Cornell’s Biomedical Engineering Ushers in a New Era of Medical Research

Biomedical engineers use the tools and principles of engineering to solve problems in medicine. Research in biomedical engineering (BME) is usually focused on prevention, diagnosis, and treatment of human disease. The human urge to be a biomedical engineer is ancient; early humans produced instruments for healing, such as flint tools that were used to gain access to the brain and splint materials that were used to support broken bones. Modern BME, which was formally organized in the 1960s, has produced some of the most important medical breakthroughs of the twentieth century, including MR and CT scanners, kidney dialysis, and artificial joints. Society anticipates . . . that biomedical engineers will produce even more advances in human health during this century.

Cornell has a long history of excellence in both the life sciences and engineering. For example, Cornell awarded the nation’s first university degree in veterinary medicine and the first doctorates in both electrical engineering and industrial engineering. Cornell also has a distinguished history of research in BME. In the past, this research emerged from individual investigators in academic units from almost every location on the Ithaca campus. The obvious places were the Colleges of Engineering and Veterinary Medicine. However, the Colleges of Arts and Sciences, Agriculture and Life Sciences, and Human Ecology also hosted important aspects of BME innovation, with the result that BME at Cornell can be regarded as a campuswide activity.

Today, the Ithaca campus stands on the threshold of a new era in BME, as does the world. This new era will support continued growth in the number of professional biomedical engineers, but it will also generate a fundamental change in the nature of the enterprise. Part of this change tracks closely the spectacular increase in the quantity of biological knowledge and the sophistication of modern biological techniques; it is now possible to manipulate, design, and control biological systems in unprecedented ways at the molecular level. In addition, a new academic discipline of BME is emerging that incorporates its own core engineering and design principles. How will these changes impact research on Cornell’s Ithaca campus?

Bridging basic biology, medicine, and engineering, an interdisciplinary group of Cornell faculty is identifying new ways to direct the formal education of students in BME, which will provide the foundation for the new era in BME at Cornell. This effort will have an important impact across campus. Biomedical engineers will act as a conduit for transferring life science concepts into engineering and engineering approaches into life sciences.

Cornell’s research strengths lie in areas of biomedical mechanics, nanobiotechnology, drug delivery, genomics/bioinformatics, and biomaterials. These areas have a significant impact on medicine. Biomedical mechanics is a longstanding specialization at Cornell with Donald Bartel, Mechanical and Aerospace Engineering, as leader. This program includes the most significant collaborative efforts between Cornell’s Ithaca campus and the Weill Cornell Medical College in New York City.

Nanobiotechnology uses the processing techniques of advanced materials to produce nanoscale devices and designs for medicine. Cornell has the most advanced program in nanobiotechnology in the United States. It has broad support with major grants from the National Science Foundation and the Keck Foundation.

Drug delivery is a research activity that has grown within the School of Chemical Engineering, where the new Program in Drug Delivery is headquartered. It, now, includes components in Materials Science, Veterinary Medicine, and Biological and Environmental Engineering. Genomics/bioinformatics and biomaterials are important branches of the campuswide efforts in genomics and materials science.

The interdisciplinary structure of BME at Cornell promotes its rapid growth and integration into the life of the university. It catalyzes new and unanticipated interactions among biologists, medical scientists, and engineers.
Biomedical Mechanics

Biomedical mechanics is a three-pronged effort involving faculty members in Mechanical and Aerospace Engineering who specialize in mechanobiology of bone (Marjolein van der Meulen), neuromuscular control of the skeletal system (Francisco Valero-Cuevas), and the analysis and design of bone-implant systems (Donald Bartel). Van der Meulen’s research is essential for determining the response of bones and bone tissue to changes in the mechanical and biological environment. Understanding these fundamentals is crucial for understanding diseases such as osteoporosis and for discovering how bone responds in the presence of implants.

Valero-Cuevas concentrates on the mechanics and control of the hand. His research ranges from evaluating the basic mechanics of hand function in the clinical setting to determining which regions of the brain are involved with basic hand function. His research team develops new ways to quantify the functional loss of the hand when particular muscles have been lost. The researchers evaluate current surgical procedures based on their ability to restore function. They propose new procedures to maximize function in the presence of particular deficiencies.

Bartel’s research on bone-implant systems has changed emphasis from the performance of individual prosthetic components to the performance of the system. The aim is to determine the relative influence of patient and surgical variables on performance compared to the influence of design variables. His goal is to find robust component and procedural designs that are insensitive to patient and surgical variables beyond the control of engineers and surgeons.

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Nanobiotechnology

Nanofabrication, a recent area of advanced technology, uses modern physical and chemical techniques to create nanoscale devices. Cornell biomedical engineers develop nanofabrication devices to solve medical problems. They use the insight gained from these devices to develop new technologies for diverse applications. For example, Cornell researchers use nanofabrication to investigate neural computation in the living brain in order to understand the efficient computational mechanisms of living organisms. Later, they will use this knowledge to develop a new class of microrobotic devices with medical applications.

In collaboration with the Wadsworth Laboratory of the New York State Department of Health, Cornell researchers use nanofabrication technology to develop neural prosthetic devices for insertion into the brain to enable long-term measurement or manipulation of central nervous system function. A multidisciplinary team of chemical and materials engineers, applied physicists, and neurobiologists are developing devices for the brain that would have microscopic drug delivery systems included in the structure, electrical input-output ports, and would be benign to the subject (minimal reactive response of the body to insertion of a foreign object). All these research activities can be characterized within the new area of advanced technology called nanobiotechnology.

Other active nanobiotechnology programs include topographical and chemical patterning of surfaces. The surfaces are used to control and manipulate cellular growth and attachment. This technology is the basis for creating artificial microenvironments that can accentuate cell growth for tissue engineering applications.

Microdevices for measurement of electrical activity in the brain. These 1-mm probes can be inserted into the tissue to allow direct measurement of local cell function.
Drug Delivery

The Cornell Program in Drug Delivery specializes in developing new drug delivery methods for treating human disease. The work utilizes modern materials science, particularly the development of biocompatible polymers that can be used to administer drugs, and focuses the action of the drugs on cells or tissues that need treatment. By targeting drug delivery—delivering the drug to the site of disease and not to the entire body—the effectiveness of the drug therapy is improved and side effects are reduced or eliminated. The research challenge is to find combinations of drugs and materials that are effective and safe in the context of a particular disease. Since diseases occur in many different tissues and organs, the design of new delivery methods must often account for the normal function of the body as well as the pattern of disease progression.

To achieve a productive union between drugs and new devices, an understanding of materials and physics is necessary but not sufficient. A quantitative understanding of the physiological processes related to drug transport, drug action, and drug metabolism is equally important. The most important goal of Cornell’s Program in Drug Delivery is training individuals to explore the link between (1) the design of molecular drugs and drug delivery systems and (2) the biology of drug metabolism and distribution in tissues.

One area of key interest is DNA delivery. Although DNA delivery is vital to the success of modern molecular medicine, current methods for safe and efficient DNA delivery, without viruses, are inadequate. Cornell scientists and engineers, however, have a long history of innovation in DNA delivery. The development of the “gene gun” in the early 1980s revolutionized the science of genetic engineering and ushered in the age of genetic transformation in the United States and the world. This pioneering advance was developed by Cornell plant scientists at the New York State Agricultural Experiment Station at Geneva, New York, and researchers and engineers at the Cornell Nanofabrication Facility (CNF).

Developing systems that are useful in medicine is Cornell’s current thrust in DNA delivery. Mark Saltzman, Chemical Engineering, and his research group conduct research in nonviral DNA delivery. Their goal is to devise synthetic, inexpensive, safe, and highly efficient DNA delivery systems that can be used in research laboratories and clinical settings. Since different medical situations require different DNA delivery systems, Saltzman’s laboratory has developed various-sized DNA delivery systems, including millimeter-sized discs, micrometer-sized spheres, nanometer-sized particulates, and molecular polymer conjugates. Most of these systems are based on polymeric materials that are biocompatible, biodegradable, and accessible. Some of these systems are being tested currently in delivery of immuncontraceptive DNA vaccines to prevent unwanted pregnancy.

Cornell’s BME effort in DNA delivery was enhanced significantly this year with the arrival of Dan Luo, a new faculty member in Biological and Environmental Engineering. Luo uses nucleic acid engineering, nanobiotechnology, cell biology, and computer simulation to study and overcome major cellular barriers of DNA/protein delivery. This enables the development of novel delivery devices that can be applied to both biological and medical research.

Genomics/Bioinformatics

Genomics is the set of computational and experimental tools that allow scientists to determine the sequence of nucleotides, or letters, that correspond to the genetic blueprint of life. A genome is an organism’s total inheritable DNA. Scientists now have the complete genomic information for more than 50 organisms, including humans. The primary challenge is to relate this information to the structure and physiology of an organism—a process known as “Functional Genomics.” Engineers play a twofold role.

One role is to enable more rapid analysis of DNA sequences of messenger molecules made from DNA and of the proteins made from the messages. Engineers build instruments that allow the rapid separation of the molecules or fragments of the molecules into individual components that can be detected and characterized. Techniques based on microfabrication or nanofabrication processes are essential for constructing such an instrument. Kelvin Lee, Chemical Engineering, develops techniques that allow the isolation and identification of many of the proteins in a biological fluid or tissue (known as proteomics). Working with Norman Relkin, Weill Cornell Medical College, Lee will use this technique for the diagnosis of neurodegenerative diseases such as Alzheimer’s. To understand the relationship of the genome to physiology requires a knowledge of time-dependent changes in messenger molecules and proteins, therefore techniques to measure all these elements are necessary.

The second role that engineers and computer scientists play is to interpret and organize genetic information through mathematical models and computer programs. The focus of bioinformatics is to identify single genes and the function of the corresponding gene product (usually a protein). Computer techniques that allow investigators to rapidly compare genetic sequence information across species have assisted in identifying the function of many genes. In other cases, investigators may deduce the function of a protein by predicting a protein’s structure from the sequence of building blocks (amino acids) that corresponds to the nucleotide sequence of the gene. Ron Elber, Computer Science, designs algorithms for computational studies to predict protein structure, dynamics, and function.
At a much different scale, researchers can apply computational techniques to gain a more complete understanding of the relation of a genome to cellular physiology. Michael Shuler’s research group, Chemical Engineering, in collaboration with David B. Wilson, Molecular Biology and Genetics, is developing a model of a “minimal cell.” Even if researchers know all the proteins that correspond to each gene in the genome, they also need to understand how these proteins form metabolic networks, how they are organized (cellular structure), and how the reactions in the cell are regulated. The minimal cell approach determines what functions are essential to a living cell and then seeks to predict what a corresponding genome must be to yield such functions. This approach is complementary to the traditional bioinformatics approach, which moves from genome to function.

The engineering effort in functional genomics and bioinformatics is an important component of a broad, campuswide venture in genomics. Interaction among researchers in engineering, computation, and the life sciences is critical to success, and Cornell has the diverse intellectual environment to support such efforts.

Educational Programs in Biomedical Engineering

New educational programs will provide the foundation for the new era in BME at Cornell. Programs of study will encompass the breadth of modern BME, while retaining the depth and rigor that have long characterized undergraduate engineering education at Cornell. Cornell faculty from across the university have identified an integrated set of core courses that will serve multiple functions: (1) an integrated undergraduate minor in BME for engineering students, with emphasis on cellular and molecular biology, (2) an integrated Program of Study in BME for biology students, (3) support for a BME concentration within the Biological and Environmental Engineering curriculum, and (4) the core of a specialized five-year program (B.S., M.Eng.) that will provide entry-level skills for the profession of biomedical engineering as well as the backbone for further studies at the doctoral level.

Although Cornell has pursued research and teaching in BME (and other areas of bioengineering) for almost 50 years, the university's formal educational programs in BME are young. In March 1997, New York State approved the Graduate Field of Biomedical Engineering (M.S./Ph.D.), which matriculated its first students in August 1998; one year later, the College of Engineering initiated a formal minor in BME for undergraduates. In addition to these new programs in BME, Cornell’s Department of Biological and Environmental Engineering (BEE) in the College of Agriculture and Life Sciences offers a B.S. concentration in biological engineering. This long-standing and highly ranked undergraduate program trains students in biology-based engineering. A unique and powerful aspect of Cornell’s present plan for BME education is the coordination of effort among faculty members in the College of Engineering and BEE. This cooperation and integration allows the university to offer undergraduate engineering students clear and distinct paths for training in BME, while taking advantage of Cornell’s institutional strengths as both a premier private research university and New York State’s land-grant university.

Cornell is uniquely positioned to build a comprehensive and influential educational program integrating medicine and engineering. The College of Engineering is accompanied by broad strength in the life sciences—spanning all scales from molecules to ecosystems and genes to behavior—and bridging several colleges: Arts and Sciences, Human Ecology, Veterinary Medicine, and Agriculture and Life Sciences. In addition, Cornell’s Ithaca campus benefits from collaborations with the Weill Cornell Medical College and the Hospital for Special Surgery in New York City. By using Cornell’s collective resources to build new educational programs and by linking education closely with present strengths in BME research, Cornell will train the next generation of engineers and medical scientists in an integrative fashion, weaving physics, chemistry, mathematics, and biology into the fabric of engineering education, and blending classroom and laboratory experiences to achieve that integration.
Biomaterials

Cornell has long been a leader in materials science and engineering. This experience allows Cornell faculty to make rapid progress in the development of new materials for medicine such as the drug delivery systems covered here.

C. C. Chu, Textiles and Apparel, has an active research program centered on the design and synthesis of biomedical materials. Currently, Chu is most excited about designing new materials with biological activity (such as nitric oxide), about biomaterials as the delivery vehicles for drugs, and about biomaterials as substrates for tissue engineering. The new biomaterials, with nitric oxide function, are synthesized from both synthetic biodegradable polymers (such as aliphatic polyesters) and hybrids of synthetic and natural-based biodegradable polymers (such as polyester-amides derived from nontoxic α-amino acids).

Nitric oxide is a very small but highly reactive and unstable free radical with many known biological functions. However, the molecule itself is extremely short lived, lasting about 6 to 10 seconds. Chu and his coworkers have created biodegradable materials that possess long-lasting nitric oxide function, which may be useful for reducing the incidence of stent restenosis after balloon angioplasty procedures in heart-attack patients. Stent/balloon procedures suffer a restenosis rate of about 40 percent due to excessive growth of tissue into stents.

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Medical Research in the College of Arts and Sciences Yields Insights on Cancer and Its Treatment

Research in the College of Arts and Sciences is designed to increase fundamental understanding of the world around us, but this emphasis on understanding does not exclude practical applications. Research on cancer, for example, has yielded important insights into such basic biological processes as cell growth and development and the flow of biological information along molecular pathways. Understanding these processes in detail can ultimately lead to the development of useful drugs for the treatment of cancer, and one group of Cornell researchers is working to translate an improved understanding of cancer into useful treatment.

Cancer develops when accumulated errors in a cell’s genetic material lead to unregulated cellular proliferation. The various forms of cancer reflect different mutations and different cellular locations, but all cancers originate from damaged genes. Typically, the damaged genes that lead to cancer involve cell signaling pathways, along which information is passed from molecule to molecule in a cell. Figure 1 shows a typical cellular signaling pathway. An external signal tells a cell to grow or to stop growing and specialize (differentiate). The information in the external signals goes from molecule to molecule along a complex network of molecular interactions. A frequent cause of cancer is a mutation in one of the proteins along the signaling pathway. Mutations that cause the growth signal to persist can lead to the unregulated cell growth that is the hallmark of cancer. Once the mutated signaling protein has been identified, a small molecule—a drug—that corrects the faulty signal can, in principle, be designed and synthesized.

For more information: http://biomedeng.cheme.cornell.edu