1
Introduction to Emerging Areas in Bioengineering

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1.1
Biotechnology

“Biotechnology” was used first time by Hungarian engineer Karoly Ereky in 1919 and refers to the use of living systems and organisms to develop or make products, or “any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use” (UN Convention on Biological Diversity, Art. 2) [1, 2].

The concept of “biotech” or “biotechnology” encompasses a wide range of procedures for modifying living organisms according to human purposes, going back to domestication of animals, cultivation of the plants, and “improvements” to these through breeding programs employing artificial selection and hybridization. Modern biotechnology, in contrast, includes genetic engineering as well as cell and tissue culture technologies based on vast genome resources of human and other living things. Depending on the tools and applications, it often overlaps with the related fields of biochemical, bioengineering, biological engineering, biomedical engineering, biomolecular engineering, biomanufacturing, etc.

1.1.1
Short Histories

Humans domesticated crops around 10,000 BC and animals, at 8000–9000 BC. At 6000 BC, we brewed beer and leavened bread at 4000 BC, long before the emergence of modern science and technology. Zymotechnology emerged to improve industrial production of beer in Germany because brewing contributed to the gross national product as much as steel, and taxes on alcohol were significant sources of revenue to the government.

In the early twentieth century, scientists gained a greater understanding of microbiology and explored ways of manufacturing specific products. In 1917, Chaim Weizmann first used a pure microbiological culture in an industrial process, using *Clostridium acetobutylicum*, to produce acetone, which was

Emerging Areas in Bioengineering, First Edition. Edited by Ho Nam Chang.

urgently needed by the United Kingdom to manufacture explosives during the World War I (WWI).

Biotechnology has also led to the development of antibiotics. In 1928, Alexander Fleming discovered the mold *Penicillium*. His work led to the purification of the antibiotic compound produced by the mold by Howard Florey, Ernst Boris Chain, and Norman Heatley to the production of what we today know as penicillin. Perhaps penicillin production was the first event of a chemical engineer's involvement during the WWII (1945). Between 1945 and 1970 many industrial biotech products, antibiotics, amino acids, and industrial enzymes, were produced using bona fide scale-up technology.

The field of modern biotechnology is generally thought of as having been born in 1972 when Paul Berg (Stanford University) created the first recombinant DNA molecules by combining DNA from the monkey virus, SV40, with that of the lambda virus. In 1973 Herbert Boyer (University of California, San Francisco) and Stanley Cohen (Stanford University) created the first transgenic organism by inserting antibiotic resistance genes into the plasmid of the bacterium *Escherichia coli* [3].

1.1.2
Application Areas

Biotechnology can be generally divided into four colored application areas: medical biotechnology (red), agricultural biotechnology (green), industrial biotechnology (white), and marine/aquatic biotechnology (blue) (Figure 1.1). In addition to the above four, environmental biotechnology (gray) and forensic

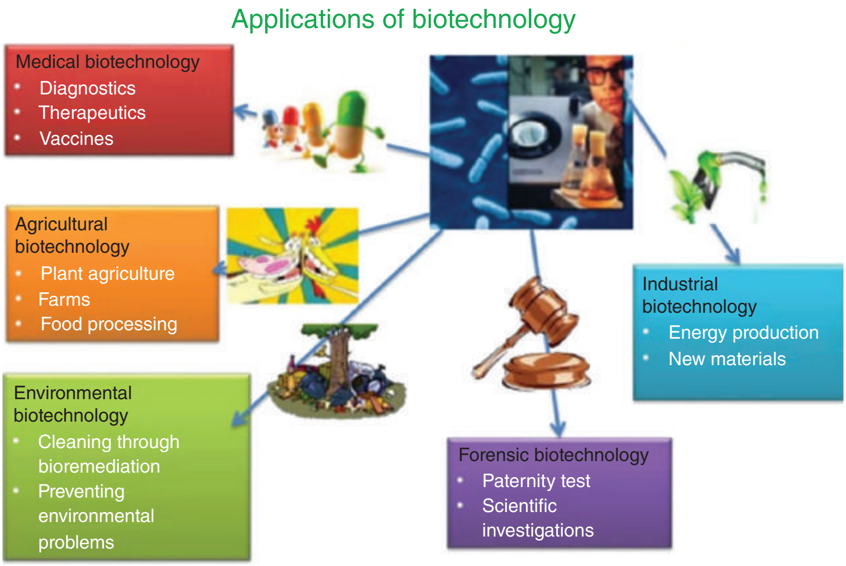

Figure 1.1 Application areas of biotechnology [4].

biotechnology can be added [4]. The listing appears to be strongly dependent on market size. The potential of aquatic (marine and freshwater) biotechnology may become very large; however, it is in its infancy from the viewpoint of the market size.

1.1.3
Markets and Industries

Figure 1.2 shows eight areas of biotechnology industry from old agriculture, pharmaceutical, and chemicals to recently evolving information technology industries. All these areas of biotechnology industries are growing rapidly and information-based biotechnology industries are newly evolved. [5].

In terms of industry category, "health" has the most market share at 51%, followed by "agriculture" (12%), industrial processing (9%), food and beverages (8%), environment (6%), bioinformatics (4%), natural resources (1%), and the rest (9%).

In medical biotechnology, the United States owns 41.0% of the market share, followed by Japan (11.5%), Germany (6.8%), France (4.8%), United Kingdom (3.9%), Korea (3.7%), China (3.1%), Canada (2.6%), the Netherlands (2.4%), Spain (1.8%), and others (18.3%).

Biotechnology firms by application in its curriculum: pharmaceutical (20%), biofuel (15%), environmental (15%), medical lab (15%), food (15%), regulatory (10%), and forensics (10%).

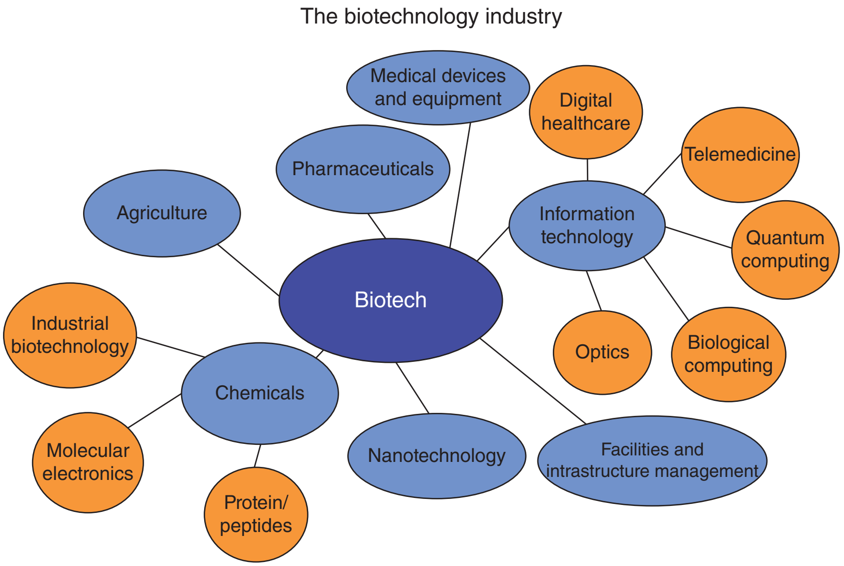

Figure 1.2 Various areas of biotechnology industries: chemicals (industrial biotechnology, proteins, and peptides), agriculture, pharmaceuticals, medical devices and equipment, information technology (digital healthcare, telemedicine, optics, biological computing, quantum computing), facilities and infrastructure management, and nanotechnology [5].

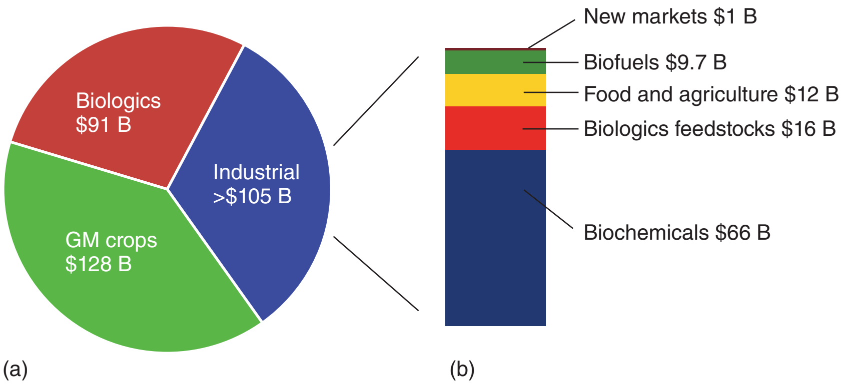

Figure 1.3 Three major biotech markets: (a) three sectors and (b) segmental industrial markets [6].

Biotechnology markets can be divided into three sectors: biologics ($91 billion (B)), industrial (greater than $105 B), and GM crops ($128 B) [Figure 1.3]. Industrial sectors can be divided further into five subsectors of biochemical ($66 B), biologics feedstocks ($16 B), food and agriculture ($12 B), biofuels ($9.7 B), and new markets ($1 B). The above listings come from the Google Image with appropriate keywords such as “application areas of biotechnology or biotechnology markets” [6].

1.1.4
Scope of Biotechnology

Agriculture lists eight important selected tools: plant breeding, biotechnology, conservation of tillage, integral pest management, sustainable resource management, variety selection, organic farming, and indigenous knowledge. Among these biotechnologies, one of eight tools may play a leading role in business. In practice genetic modification or genetically modified organism (GMO) is considered as the most important product and tool in biotechnology or understanding of genetics information [6]. Classical biotechnology was simple and less costly, while modern biotechnology becomes more complex and costly.

1.2
Bioengineering

1.2.1
History of Engineering

Engineering [7, 8] differs from science disciplines in terms of dealing with systems and their overall economic optimizations. It is the application of mathematics, empirical evidence, and scientific, economic, social, and practical knowledge in order to invent, design, build, maintain, research, and improve structures, machines, tools, systems, components, materials processes, and organizations. The discipline of engineering is extremely broad and encompasses a range of more specialized fields of engineering, each with a more specific emphasis on particular areas of applied science, technology, and types of application. The term *engineering* is derived from the Latin *ingenium*, meaning "cleverness," and *ingeniare*, meaning "to contrive, devise." Engineering requires economy, public reliability, and responsibility, while scientific discovery remains sometimes private.

Four major categories of engineering are electrical, mechanical, chemical, and civil engineering. And later industrial engineering, computer science and engineering, and materials science and engineering were added to the schools of engineering. Recently bioengineering, biological engineering, and biosystems engineering are added as medical biotechnology becomes progressively important.

1.2.2
Two Different Bioengineering

The mass production of penicillin during the WWII was started in the United States with participation of chemical engineers [9]. Since then many new antibiotics, amino acids, and enzymes were produced in large quantities. In order to cover this need, the first issue of "Biotechnology and Bioengineering" was published in 1959. This time "biotechnology" meant mostly "applied microbiology," and "bioengineering" meant "bioprocessing of microorganisms" by chemical engineers and called as "biochemical engineering."

Another "bioengineering" meant "biomedical engineering" in late 1960s and early 1970s to understand physiological change of astronauts during their space travels. Many universities in the United States were funded under the "bioengineering" program.

The first "bioengineering" is still used as research area of chemical engineering departments, but rarely or none as department name, while the second "bioengineering" is used as a department name of biomedical engineering. Furthermore Merriam-Webster defines that bioengineering is the "biological or medical application of engineering principles or engineering equipment" – also called biomedical/biological engineering.

1.2.3
Chemical Engineering

The industrial revolution (mid-eighteenth and late nineteenth century in Scotland and United Kingdom) led to escalation in demand, both with regard to quantity and quality, for bulk chemicals such as soda ash [10]. This meant two things: one, the size of the activity and the efficiency of operation had to be enlarged and, two, serious alternatives to batch processing, such as continuous operation, had to be examined.

1.2.3.1 The First Chemical Engineer

Industrial chemistry was being practiced in the mid-1800s, but it was not until the 1880s that the engineering elements required to control chemical processes were being recognized as a distinct professional activity. Chemical engineering was first established as a profession in the United Kingdom when the first chemical engineering course was given at the University of Manchester in 1887 by George E. Davis. The American Institute of Chemical Engineers (AIChE) was founded in 1908, and the U.K. Institution of Chemical Engineers (IChemE) was founded in 1922.

Starting from 1888, Lewis M. Norton taught the first chemical engineering course at Massachusetts Institute of Technology (MIT). Arthur D. Little of MIT emphasized the approach of unit operations and unit processes since chemical processes consist of a series of reactions and separation processes to achieve a desired product, having required quality from a given raw material [11]. The concept has even been used today to understand the functions of the human body. In order to understand major engineering department better, mechanical engineering meant machines, electrical engineering meant circuitry, and civil engineering meant structures. Therefore, chemical engineering can be symbolized as chemicals production and today's biological engineering means much more than making biochemicals.

1.2.4
Biochemical Engineering (1945–1978)

Biochemical engineering, also known as *biotechnology engineering* or *bioprocess engineering*, is a branch of chemical engineering that mainly deals with the design and construction of unit processes involving biological organisms or molecules, such as bioreactors. Its applications are in the petrochemical industry, food, pharmaceuticals, biotechnology, and water treatment industries. It is taught as a course in chemical engineering departments or departments of chemical and biochemical engineering [12].

1.2.4.1 Penicillin Production

The effects of *Penicillium* mold was finally isolated by Scottish scientist Alexander Fleming on the morning of September 28, 1928 [13]. The traditional version of this story describes the discovery as a "serendipitous accident": in his laboratory in the basement of St Mary's Hospital in London (now part of Imperial College). In 1939, Australian scientist Howard Florey (later Baron Florey) and a team of researchers (Ernst Boris Chain, Arthur Duncan Gardner, Norman Heatley, M. Jennings, J. Orr-Ewing, and G. Sanders) at the Sir William Dunn School of Pathology, University of Oxford, made progress in showing the *in vivo* bactericidal action of penicillin. In 1940, they showed that penicillin effectively cured bacterial infection in mice. In 1941, they treated a policeman, Albert Alexander, with a severe face infection; his condition improved, but *then supplies of penicillin ran out and he died*. Subsequently, several other patients were treated successfully.

1.2.4.2 **Mass Production of Penicillin**

By late 1940, the Oxford team under Howard Florey had devised a method of mass-producing the drug, however the yields remained low [14]. In 1941, Florey and Heatley traveled to the United States in order to interest pharmaceutical companies in producing the drug and inform them about their process. Florey and Chain shared the 1945 Nobel Prize in Medicine with Fleming for their work.

The challenge of mass production of this drug was daunting. On March 14, 1942, the first patient was treated for streptococcal septicemia with the U.S.-made penicillin produced by Merck & Co. Half of the total supply produced at the time was used on that one patient. In June 1942, just enough U.S. penicillin was available to treat 10 patients. In July 1943, the War Production Board drew up a plan for the mass distribution of penicillin stocks to the Allied troops fighting in Europe. The results of fermentation research on corn steep liquor at the Northern Regional Research Laboratory at Peoria, Illinois, allowed the United States to produce 2.3 million doses in time for the invasion of Normandy in the spring of 1944. After a worldwide search in 1943, a moldy cantaloupe in a Peoria, Illinois, market was found to contain the best strain of mold for production using the corn steep liquor process. Large-scale production was carried out in a deep-tank fermentor designed by chemical engineer Margaret Hutchinson Rousseau. As a direct result of the war and the War Production Board, by June 1945, over 646 billion units per year were being produced.

After WWII, Australia was the first country to make the drug available for civilian use. In the United States, penicillin was made available to the general public on March 15, 1945.

Margaret Hutchinson Rousseau (October 27, 1910–January 12, 2000) was a chemical engineer who designed the first commercial penicillin production plant [14]. She was also the first female member of the AIChE. Margaret Hutchinson was born in Houston, Texas, and received her Bachelor of Science degree from Rice Institute in 1932 and her Doctor of Science degree in chemical engineering from MIT in 1937. She was the first woman to earn a doctorate in the subject in the United States. She started her professional career during the WWII and oversaw the design of production plants for the strategically important materials of penicillin and synthetic rubber. She also worked on the development of high-octane gasoline for aviation fuel. Her later work included improved distillation column design and plants for the production of ethylene glycol and glacial acetic acid. In 1955 she received the Achievement Award of the Society of Women Engineers. In 1983, she was the first female recipient of the prestigious Founders Award of the AIChE [15].

Pfizer, Merck, Squibb, and Lilly companies produced penicillin commercially during the WWII using deep-tank fermentation. Their contributions were summarized as follows. The cooperative efforts of American chemists, chemical engineers, microbiologists, mycologists, government agencies, and chemical and pharmaceutical manufacturers were equal to the challenge posed by Howard Florey and Norman Heatley in 1941. As Florey observed in 1949, “too high a tribute cannot be paid to the enterprise and energy with which the American manufacturing firms tackled the large-scale production of the drug. Had it not been for their efforts, there would certainly not have been sufficient penicillin by D-Day in Normandy in 1944 to treat all severe casualties, both British and American." [16].

1.2.5
Biochemical Engineering Education

United Kingdom is a country where penicillin was discovered by Scottish scientist Alexander Fleming in 1928 at St. Mary's Hospital in London [17]. In the 1930s Jack Drummond, the first professor of biochemistry at the University College London (UCL), succeeded in isolating pure vitamin A. However, to accomplish this, he needed large quantities of fish liver oils and, later, wheat germ. Drummond was helped by Maxwell Donald, a young process engineer and lecturer of chemical engineering at UCL. Thus it began the association of departments that created the Department of Biochemical Engineering. Many years later Malcolm Lilly (1926–1997) and Peter Dunnill (1938–2009) became the first professors of biochemical engineering in the United Kingdom.

Elmer L. Gaden Jr. (1923–March 10, 2012) has been described as "the father of biochemical engineering." A graduate of Columbia University, he wrote a dissertation that quantified the amount of oxygen necessary to fuel the fermentation process used to produce penicillin. Gaden established Columbia's program in biochemical engineering. He remained at Columbia for 26 years as a teacher, researcher, and department chair, before becoming dean of the College of Engineering, Mathematics, and Business Administration at the University of Vermont in 1974. In 1979, he joined the engineering faculty at the University of Virginia as the Wills Johnson Professor of chemical engineering. In 1994 he retired from Virginia, becoming Wills Johnson Professor Emeritus.

Arthur E. Humphrey (born November 9, 1927) is an American chemical engineer. He received the John Fritz Medal in 1997. He was the President of the AIChE from 1990 to 1991. He was also a former provost and the vice president of Lehigh University, serving from 1980 to 1987. Humphrey was born in Moscow, Idaho, and attended the University of Idaho, the MIT, and Columbia University (Ph.D. 1953 in Chemical Engineering). He has taught at the University of Pennsylvania and Lehigh University.

Daniel I-C. Wang (born March 12, 1936) is an Institute Professor at the MIT. Wang received the SB (1959) and SM (1961) from MIT, and the Ph.D. in chemical engineering from the University of Pennsylvania in 1963. He joined the MIT faculty in 1965 and is a member both of the National Academy of Engineering and the American Academy of Arts and Sciences. He has coauthored five books and more than 100 papers in professional journals. He founded the Biotechnology Process Engineering Center. His research on fermentation, monitoring and control of bioprocesses, renewable resource utilization, enzyme technology, product recovery and purification, protein aggregation and refolding, and mammalian cell cultures made him a pioneer in biochemical and biological engineering.

James E. Bailey (1944–2001) studied chemical engineering at Rice University receiving a BA in 1966 and Ph.D. in 1969. He worked for Shell, taught chemical engineering at the University of Houston since 1971, moved to Caltech in 1980, and became a Professor of Biotechnology at the Swiss Federal Institute of Technology (ETH) in Zurich in 1992. He died of cancer on May 9, 2001. He is a pioneer of biochemical engineering, particularly (prokaryotic) metabolic engineering. He is recognized as "the most influential biochemical engineer on metabolic engineering of modern times" [18].

He worked with more than 100 Ph.D. students and postdocs among whom about 50 are currently teaching in universities. It did not take much time for him to start his metabolic engineering program at Caltech considering that the first work on recombinant DNA (Berg, 1972), Cohen and Boyer's work on recombinant DNA (1973), and production of human growth hormone (1977) and human insulin in 1978 by Genentech founded by Boyer and Swanson in 1976.

1.2.6
Biomedical Medical Engineering Activities (before 1970)

The *stethoscope* is an acoustic medical device for auscultation, or listening to the internal sounds of an animal or human body [19]. The stethoscope was invented in France in 1816 by René Laennec at the Necker–Enfants Malades Hospital in Paris. It consisted of a wooden tube and was monaural. Laennec invented the stethoscope because he was uncomfortable placing his ear on women's chests to hear heart sounds [20]. In 1881 Samuel von Basch invented the blood pressure meter (also known as *sphygmomanometer*). In 1895, Conrad Roentgen (Germany) discovered the X-ray using gas-discharged tubes that obtain imaging of internal organs of human body.

An *artificial organ* is a man-made device that is implanted or integrated into a human – interfacing with living tissue – to replace a natural organ, for the purpose of duplicating or augmenting a specific function or a group of related functions, so the patient may return to a normal life as soon as possible. Such organs include artificial limbs, bladder, ear, eye, heart, liver, ovaries, and thumb [21]. For further details please refer to the book on tissue engineering and physiology textbook [22, 23] or visit the websites on Wikipedia on regenerative medicine and stem cells [24, 25].

Artificial kidney was first developed by Abel (1913), and further by Hass (1924) for humans. Dr Willem Kolff is considered as the father of clinical dialysis. This young Dutch physician constructed the first dialyzer (artificial kidney) in 1943 [26]. Artificial kidney is often a synonym for hemodialysis but may also, more generally, refer to renal replacement therapies (with exclusion of kidney transplantation) that are in use and/or in development. It also means bioengineered kidneys/bioartificial kidneys that are grown from renal cell lines/renal tissue that may, in the future, substitute more kidney functions other than hemodialysis, one of the many kidney functions.

1.3
Emerging Areas

1.3.1
Evolvement (Birth)

According to Thomas Kuhn (1922–1996) of Harvard University, scientific fields undergo periodic "paradigm shifts" rather than solely progressing in a linear and continuous way, that these paradigm shifts open up new approaches to understanding what scientists would never have considered valid before, and that the notion of scientific truth, at any given moment, cannot be established solely by objective criteria but is defined by a consensus of a scientific community [27].

Emerging areas in bioengineering have evolved not only from the influences of bioscience and biotechnology themselves but also from those of all sciences and technologies and will be influenced furthermore by all the currently unknown factors. These factors can be needs of current or future societies to come and available tools or capacities to meet them. In biotechnology discovery of double helix by Crick and Watson, restriction enzyme by Arthur Kornberg and Severo Ochoa (1959), recombinant DNAs by Stanley Cohen and Herbert Boyer (1973), and human genome projects (1999) played a great role in advancing generic biotechnology to current DNA-based revolutionary biotechnologies. In other words, the paradigm shifts in biology or biotechnology made possible a current revolutionary progress.

The fourth industrial revolution on biology and biotechnology will be more fruitful by employing Internet of things (IOTs), big data, three-dimensional (3D) printing, artificial intelligence (deep learning, machine learning), RFID technology, virtual reality, and tissue engineering.

1.3.2
Biological Engineering

The word "biological engineering" [28] has been used since the successful completion of Human Genome Project (1990–2013). Engineers often claim that there are three categories of discipline of science (pure), technology (applied science), and engineering. "Biological engineering" is engineering for biological science if "chemical engineering" represents engineering for chemistry. Also these two disciplines have plenty of similarities in terms of academic program and research contents. Biological reactions are covered in biological engineering like chemical reactions in chemical engineering, while the unit operations are very similar to each other in the both. Still several chemical engineering departments keep "chemical engineering and biochemical engineering" (Rutgers University, Brown University, University of Iowa). Major chemical engineering department has their names as Chemical and Biomolecular Engineering (Berkeley, Cornell, KAIST), Chemical Engineering (MIT, Stanford, Caltech), and Chemical and Biological Engineering (Princeton, Seoul National University), while the College of Agriculture of Cornell University has a Biological and Engineering Department.

Whatever your department is named, it is certain that chemical engineering department cannot discard "chemical" or may not use "biomedical" as their department name. The information on biological engineering from Wikipedia is very close to bioengineering (biomedical engineering). The contents of biological (bioengineering) engineering are as follows. Some parts of these categories are overlapped with those of major engineering departments of ChE, ME, and EES:

- Biological systems engineering and biomedical engineering: biomedical technology, biomedical diagnostics, biomedical therapy, biomechanics, biomaterials
- Genetic engineering (involving both of the above, although in different applications): synthetic biology, horizontal gene transfer
- Bioprocess engineering: bioprocess design, biocatalysis, bioseparation, bioenergy
- Cellular engineering: cell engineering, tissue engineering, metabolic engineering
- Biomimetics: the use of knowledge gained from reverse engineering that evolved living systems to solve difficult design problems in artificial systems
- Bioinformatics

1.3.3
Bioengineering/Biological Engineering in Chemical Engineering Department

The *MIT Department of Chemical Engineering* has 48 faculty members, 15 professors of which are involved in biological engineering research [29]. Here "biological engineering" is a mixture of biochemical and biomedical engineering nature. MIT chemical engineering research areas are thermodynamics and molecular computations, catalysis and reaction engineering, systems design and engineering, transport processes, biological engineering, materials, polymers, surfaces and structures, and energy and environmental engineering [30]. Professor *Robert Langer* works on the interface of biotechnology and materials science. A major focus is the study and development of polymers to deliver drugs, particularly genetically engineered proteins, DNA and RNAi, continuously at controlled rates for prolonged periods of time. Bob Langer received the Queen Elizabeth Prize for Engineering on October 26, 2015 [31]. MIT has, separately from all the other engineering departments, a department of biological engineering similar to bioengineering of other universities.

UC Berkeley has a department of chemical and biomolecular engineering that belongs to the College of Chemistry [32]. Their research areas are bioengineering (14/25 faculties), polymers and soft materials, catalysis and reaction engineering, environmental engineering/microelectronics processing and MEMS, theory, multiscale modeling, and computer simulation/electrochemical engineering. Professor Keasling is working on metabolic engineering of microorganisms. The research focuses on the metabolic engineering of microorganisms for degradation of environmental contaminants or for environmentally friendly synthesis: synthesis of biodegradable polymers, accumulation of phosphate and heavy metals, and degradation of chlorinated and aromatic hydrocarbons, biodesulfurization of fossil fuels, and complete mineralization of organophosphate nerve agents and pesticides [30].

1.3.4
Biomaterials

Two important subjects of chemical engineering are balances of materials (mass) and energy [33]. In fermentation energy is evolved even in anaerobic fermentation, which needs to be cooled by colder water. However, in general biological reaction energy is not as important as in chemical reactions. The materials in chemical engineering are diverse in molecular weight from hydrogen to uranium in atoms, molecules from hydrogen, and nitrogen gas to very high molecular weight polymers. Properties of recently revolved nanomaterials are sometimes completely different from simple molecules or high molecular polymers. Figure 1.4 shows an overview of the applications and current research into processing techniques of polymer nanofibers. The application areas in biotechnology are tissue engineering scaffolds, wound dressing, medical prosthesis, drug delivery, and cosmetics.

1.3.5
Marine Biotechnology

A large proportion of all life on Earth lives in the ocean. Exact proportion of marine life of still is unknown, since many ocean species are still to be discovered. The ocean is a complex 3D world covering approximately 71% of the Earth's surface.

Marine biology is the scientific study of organisms in the ocean or other marine bodies of water. Given that in biology many phyla, families, and genera have some

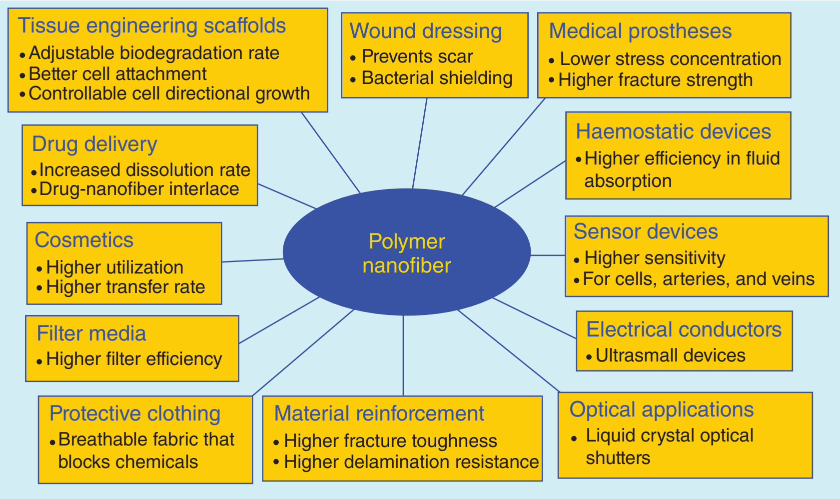

Figure 1.4 Polymer nanofiber and its application [33].

species that live in the sea and others that live on land, marine biology classifies species based on the environment rather than on taxonomy. Marine biology differs from marine ecology, as marine ecology is focused on how organisms interact with each other and the environment, while biology is the study of the organisms themselves [34].

1.3.5.1 Marine Biotechnology

Marine Board-ESF, or "the Marine Board of European Science and Foundation (ESF)," provides a pan-European platform for its member organizations to develop common priorities, to advance marine research, and to bridge the gap between science and policy in order to meet future marine science challenges and opportunities. The details are given in the position paper by the Marine Board [35].

Marine engineering includes the engineering of boats, ships, oil rigs, and any other marine vessel or structure, as well as *oceanographic engineering*. Specifically, marine engineering is the discipline of applying engineering sciences, including mechanical engineering, electrical engineering, electronic engineering, and computer science, to the development, design, operation and maintenance of watercraft propulsion, and on-board systems and oceanographic technology. It includes but is not limited to power and propulsion plants, machinery, piping, automation, and control systems for marine vehicles of any kind, such as surface ships and submarines [36].

1.3.6
Environmental Biotechnology

Environmental biotechnology is biotechnology that is applied to and used to study the natural environment and could also imply that one try to harness biological process for commercial uses and exploitation. The International Society for Environmental Biotechnology defines environmental biotechnology as "the development, use, and regulation of biological systems for remediation of contaminated environments (land, air, water), and for environment-friendly processes (green manufacturing technologies and sustainable development)" [37].

Environmental biotechnology can simply be described as "the optimal use of nature, in the form of plants, animals, bacteria, fungi, and algae to produce renewable energy, food, and nutrients in a synergistic integrated cycle of profit making processes where the waste of each process becomes the feed stock for another process."

1.3.7
Biomedical Engineering

The *Department of Biomechanical Engineering* of Delft University of Technology is a research department at the Delft University of Technology, located in the faculty of mechanical, maritime, and materials engineering (3ME). The department coordinates the education and research activities in the field of mechanical engineering techniques like modeling and design to analyze the interaction between biological and technical systems: medical instruments and bio-inspired technology, biomechatronics and human–machine control, biorobotics, intelligent vehicles and cognitive robotics, and biomaterials and tissue biomechanics [38].

MIT Electrical Engineering and Computer Science Department (EECS) develops the technologies and infrastructure of the information age – ranging from the Internet and search engines to cell phones, high-definition television, and optical system. Biomedical sciences and engineering is one of seven areas of research together with information systems, circuits, applied physics and devices, computer science (artificial intelligence), computer science (systems), and computer science (theory). *Bioscience* (including both fundamental biology and medicine) is arguably the most important engineering system that mankind wishes to model, understand, and engineer. EECS provides a rich set of analytical tools to tackle these systems [39].

"*MIT biological engineers*" have devised a way to record complex histories in the DNA of human cells, allowing them to retrieve "memories" of past events, such as inflammation, by sequencing the DNA. This analog memory storage system – the first that can record the duration and/or intensity of events in human cells – could also help scientists study how cells differentiate into various tissues during embryonic development, how cells experience environmental conditions, and how they undergo genetic changes that lead to disease [40].

The *Bioengineering Department* of John Hopkins University has 41 faculty members and their research areas are biomedical imaging, cell and tissue engineering, computational biology, computational medicine, molecular and cellular systems biology, systems neuroscience, and neuroengineering. "The brain is perhaps the greatest and most complicated learning system and exercises control over virtually every aspect of behavior. Investigators in this area share a common desire to produce quantitative models of information coding and processing in neural systems." Professor Thakor studies development of novel microfabricated sensor and devices for neuroscience research using MEMS (microelectromechanical) techniques that allow us to grow neurons and neural networks on a chip (neurochip) [41].

Stanford University Bio-X Initiative is part of Stanford University and is located in the James H. Clark Center in Stanford, California, adjacent to Palo Alto and Menlo Park [42]. With over 200 medical device companies within 20 miles and three top-tier hospitals within walking distance, the Stanford campus provides a unique setting for medical innovation. The program brings biomedical and life science researchers together with engineers, physicists, and computational scientists to tackle the complexity of the body in health and disease. The major theme of Bio-X is to unlock the secrets of the human body by treating body and brain as a whole assembly of complex organ systems that interact with each other dynamically. To succeed in this mission, every tool in the scientists' tool kit is needed, and we need to invent new tools. The faculty should represent all areas of science and technology, making significant discoveries, inventing, and training future generations of scientists.

1.3.8
Multidisciplinary (OMICS) Approach

OMICS International (and its subsidiaries) is an open access publisher and international conference organizer, which owns and operates 700 peer-reviewed clinical, medical, life sciences, and engineering and technology journals and hosts 3000 scholarly conferences per year in the fields of clinical, medical, pharmaceutical, and life sciences, business, engineering, and technology. Our journals have more than 15 million readers and our conferences bring together internationally renowned speakers and scientists to create exciting and memorable events, filled with lively interactive sessions and world-class exhibitions and poster presentations. Here biomusical engineering and journal of bioterrorism and defense are introduced [43].

1.3.8.1 Biomusical Engineering

Dorita S. Berger, Editor in Chief of Biomusical Engineering, writes about the scope of this journal: “Research on music in the sciences and medicine is finally reaching the forefront of attempts to understand the brain, cognition, physiology, and emotional behaviors. Because of the birth of such scientific and engineering music explorations, this unique Journal of Biomusical Engineering has been put forth as a new platform for researchers and philosophers in and about music in human adaptation, to publish their thoughts and findings and reach a whole new, cross-modal audience of readers from music anthropology to musicology, from music composition and expression to music-based treatment modalities” [44].

1.3.8.2 Journal of Bioterrorism and Defense

The journal considers different topics under the biodefense and bioterrorism subject. Particularly, this periodical seeks submissions on the following topics: anthrax bioterrorism, biosurveilliance, biodefense, biohazards, biological preparedness, biowarfare, biological weapons, biorisk, bioterrorism agents, biothreat agents, disease surveillance, emerging infectious disease, nuclear terrorism, U.S. biological defense program, vaccines, and probabilistic risk assessment [45].

1.4
Current Volume

Google Image search on the “fourth industrial revolution” is shown Figure 1.5. However it does not cover much on biotechnology itself [46].

The fourth industrial revolution will have a tremendous impact on car industry such as in autonomous driving [47] and AI-operated robots [48]. Robots and devices equipped machine learning capability can accumulate more data and

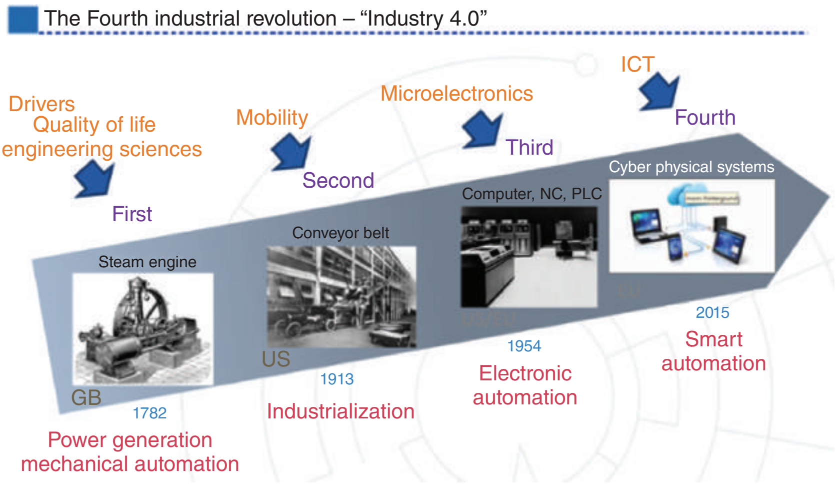

Figure 1.5 The fourth industrial revolution – industry 4.0 [46].

handle more complex systems without human help and make a decision based on its own knowledge [49]. Google Image search also picked seven areas of the fourth industrial revolution on genetics, nanotechnology, biotechnology, IOTs, quantum computing, artificial intelligence, and 3D printing. Additionally, big data may be added.

Biotechnology includes AI-based diagnostics of diseases such as IBM Watson [50] using big data and personalized prescription as well as bioplant based on IOTs and its management using mobile system. In the future "deep learning" may help synthetic biologist or biotechnologists to handle more complex biological metabolic network systems. All of these advanced technologies may create more new jobs or eventually eliminate older jobs. One thing we know at this moment is that large control system based on current ICT may be handled by software imbedded machines and equipment in a near future.

Google Image search shows that current world biotech market volume (2016) is 140 billion USD, and it will increase to 240 billion USD with an annual growth rate of 11.55%. While for world cosmetics industry, it is 53.76 USD, corresponding to 38.4% of the biotech revenue [51, 52]. Industries of antiaging, functional foods, and beauty may grow faster than the others.

This volume consists of 10 chapters with similar contents: reaction engineering (6), bioenergy (6), synthetic biology applications (6), biomaterial and cosmetics (2), chemicals from biomass (3), drug delivery (5), bioprocess simulation (5).

Acknowledgments

I would like to thank all the authors, chapter coordinators, and Claudia Ley of Wiley for their contribution of manuscripts and helping me make this volume possible: Biosensor and Nanoparticles (HG Park, KAIST, Korea), Enzyme

Reaction Engineering (WC Lee, National Cheng Kung U, Taiwan), Drug Delivery (SK Han, Postech; YR Byun, Seoul National U), and Bioprocess Simulation (CH Lee, SNU, Korea).

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