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The Evolution of Biological Engineering*

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The discipline of Biological Engineering is an academic structure evolving to address educational needs based on technologies arising from the new advances in the life sciences. This paper focuses on presenting concepts that distinguish Biological Engineering as a discipline, distinct from existing engineering disciplines, based on unique principles that define biology/living systems. It presents a perspective of Biological Engineering that focuses on the engineering of the inherent, central principles of living systems versus the application of externally engineered systems to existing living systems to alter their behavior or structure. Important concepts in educational curricular topics and concepts are also discussed, along with the historical background to the development of Agricultural Engineering into Biological Engineering.

Keywords: biological engineering; agricultural engineering; historical overview; living systems

INTRODUCTION

RECENT ADVANCES WITHIN the life sciences have changed the way we view biology and engineering. The ability to quantitatively measure and model life processes is rapidly advancing historically descriptive biology, to become a basis for engineering design and innovation. Interestingly, agricultural engineers recognized the need for this information almost a century ago but lacked the basic scientific foundations upon which to base biological engineering principles. Today we anticipate that, within a few decades, these unique fundamental principles of how living systems work will be much more extensively established and Biological Engineering will emerge as a significant new discipline for the future. Commensurate with biology becoming the basis for a new engineering discipline is the need for a different kind of engineering education. Purdue University's Department of Agricultural and Biological Engineering is actively pursuing the development of this educational model to meet the current and future demands of this fundamental new engineering discipline.

Historically, engineering disciplines have been developed to reflect the rational harnessing of a core science, such as physics or chemistry, along with mathematics, in response to meeting societal needs. Current engineering disciplines, such as civil, mechanical, and electrical engineering, are based primarily on physics, while chemical engineering incorporates chemistry. The more narrowly defined disciplines of petroleum, mining, ceramic, aeronautical, food process, nuclear, agricultural, and aquatic engineering reflect tailored interests to very specific industries. While biology is mechanistically dependent upon both chemistry and physics, it incorporates many unique features that distinguish it as a core science. In this article, we describe our definition of Biological Engineering (BE) and the current and developing BE curricula at Purdue University, and discuss the evolution of Biological Engineering as a new discipline.

HISTORY OF ENGINEERING

The use of scientific principles to solve practical problems is a key characteristic of engineering. Some notable early engineering marvels include the architecture, pyramids, land monuments, and irrigation and canalling practices that came into existence around 2750 BC [1]. Egyptian epitaphs, as well as existing landmarks, exemplify the work of this time. The ancient Greeks had a different approach to engineering, concentrating as heavily on aesthetics as on functionality, which agreed with the significance placed on virtue at this time [2]. By 270 BC, the Greeks had created numerous mechanical, pneumatic, and hydraulic components, such as: musical instruments, clocks, springs, and water wheels to hoist water [2]. Archimedes is known to have calculated buoyancy, and centers of gravity for application in building ships at that time. At nearly the same time, the Chinese, responsible for the invention of gunpowder, were engineering underground tunnels, dams and canals for the beneficial utility of water, and 'the Appian Way' of the Romans created roads and channels still in use today.

However, with all of these examples, the word 'engineer' still does not appear in any descriptive contexts until the Middle Ages [3]. Tertullian, an early Christian author, applied the term '*novum extraneum ingenium*', meaning ingenious device, in describing battering rams in 200 AD, but the term 'ingeniator', or engineer, was coined much later to describe the originators of military devices such as crossbows, battering rams and trebuchets, during

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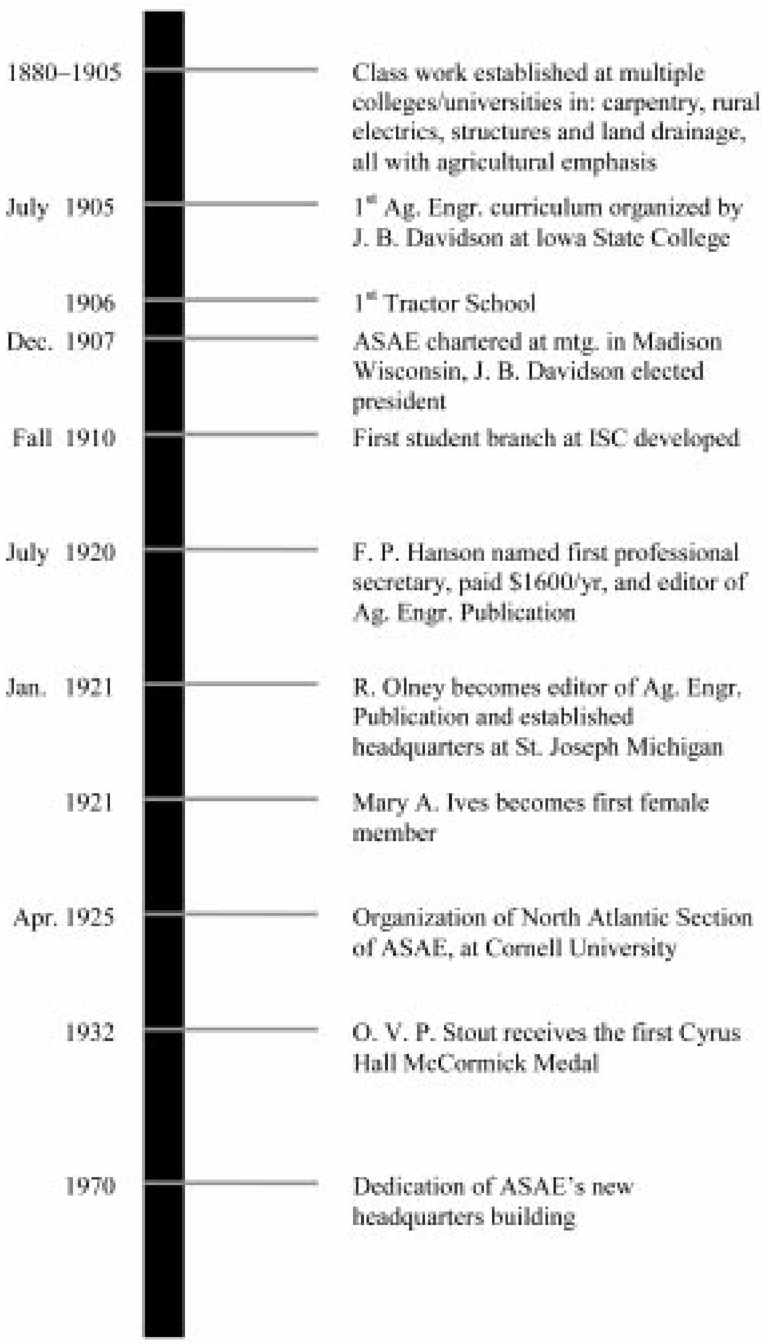

Fig. 1. ASAE timeline.

Gothic times [3]. The focus of engineering was concentrated on military achievements and agricultural development to improve food supplies. The Middle Ages also saw the conversion of many labor-intensive jobs to hydraulic, water-powered operations. Civil engineering emerged as the first non-martial, professional engineering discipline, reflected by the cathedrals, bridges and canals and the Great Wall of China, all constructed in this time period [2]. However, not all of the achievements of this era were civil engineering. Clock-making as a mechanical science was also developed, and some of the first attempts in aeronautics occurred during this time-frame.

Development of engineering as a discipline did not occur until the Renaissance era. Primarily focused around civil and mechanical engineering, numerous books recorded the technical details of the design of structures, mills, siphons and the like, indicating progress in the definition of these professions. (For a good review of some of the significant contributions to the Industrial Revolution, see http://www.knockonthedoor.com/.) The development of railroad systems greatly expanded the role of these two types of engineers. Building railroads incorporated the unique skills that civil engineers had previously employed in the design of canals and highways, as well as the science of

Table 1. Standard agricultural engineering curriculum adopted from ISC*

Subject Description	Percentage of Total Classwork
Agricultural engineering	14.2
General engineering	21.6
General agriculture	19.2
Science	28.4
Cultural subjects	5.5
Elective	8.2
Military and physical training	2.7

* Taken from [5]—no indication as to where the other 0.2% is at.

mechanical propulsion disclosed by the mechanical engineer. The emergence of mechanical engineering was further elucidated during the Industrial Revolution as steam power was harnessed for multiple uses.

Chemical engineering as a profession was not well established until near the end of the nineteenth century. Starting initially as industrial chemistry, chemical engineering saw tremendous growth when fundamental thermodynamic principles of vapor-liquid equilibrium were established to put the industrial practice of petroleum distillation on scientific foundations. Demands for petrochemicals and fuels in the mid-1900s spurred the development of chemical engineering fundamentals, such as unit operations, reaction kinetics, and transport phenomena. As post-World War Two American industries diversified into more complex processes to develop new polymers and plastics, chemical engineering enjoyed a golden era of growth. The highly analytical and abstract critical thinking structure of chemical engineering education has allowed graduates to thrive in a variety of technical and economic disciplines beyond traditional petroleum-based technologies.

HISTORY OF AGRICULTURAL ENGINEERING

The origins of agriculturally based engineering curricula can be traced back to the roots of farming itself. The Neolithic revolution that describes the transformation of hunter-gatherers into farmers occurred some 10,000 years ago [4]. At this time humankind became more settled, forming villages, domesticating animals and producing crops for subsistence. The development of tools to aid in the daily chores related to food production are the first examples of the agricultural engineering profession. At the beginning of the twentieth century, the profession of agricultural engineering was formally established with the development of the American Society of Agricultural Engineers in 1907. A comprehensive review of the history is given by R. Stewart in his book, *Seven Decades that Changed America: A History of the American Society of Agricultural Engineers* [5]. Some of the highlights are shown on the timeline of Fig. 1 and a standard topical curriculum is given in Table 1. At the beginning of the society's professional development, agriculture had progressed to encompass the use of mules for horse power, along with steam-propelled threshers and a limited number of gasoline tractors. The demands for reduction in labor to make farming more efficient resulted in the application of the mechanical arts to farming. Because most mechanical engineers had limited interest in agriculture, agricultural engineering developed to fulfill this need. To this extent, most of the charter members of ASAE were trained in either mechanical or civil engineering, but with interests in agriculture. The challenge of uniquely defining agricultural engineering would be ongoing and, as with most disciplines, it continues even today.

The first notable example of this professional society's evolution toward biology, highlighted by Stewart [5], involved C.O. Reed and took place in the 1930s. According to a disgruntled Reed, the philosophy of ASAE suggested that, 'agricultural engineering simply is the service of mechanical, civil, electrical, architectural, and industrial engineering taken to the industry of agriculture, as if we were condescending to carry to agriculture something from outside it.' Reed did not agree with this notion and put forth his own vision, distinguishing agricultural engineering as the 'engineering of biology . . . This unique kind of engineering should be based on the energy transformations and transfer conducted by living cells; a methodology and efficiency concept so based would open a new world to the agricultural engineer.' While ASAE headquarters embraced Reed's view, suggesting this would confer distinction from other engineering branches and therefore not 'step on the toes of others', apparently many members did not agree with the idea and it had died along with Reed by 1940.

By the 1960s, chemical engineering, which was founded at nearly the same time as agricultural engineering (see Table 2), had become well-defined in the area of unit operation, thanks in great part to earlier work by McCabe, the clear quantitation of vapor-liquid principles, and to transport processes

Table 2. Engineering societies founded*

Society	Founded
American Society of Civil Engineers	1852
American Institute of Mining Engineers	1871
American Society of Mechanical Engineers	1880
American Institute of Electrical Engineers	1884
Society of Naval Architects and Marine Engineers	1893
American Society of Heating and Ventilating Engineers	1894
American Railroad Engineers' Association	1897
Society of Automobile Engineers	1904
Illuminating Engineering Society	1906
American Society of Agricultural Engineers	1907
American Institute of Chemical Engineers	1908

* Taken from [5].

due to the ground-breaking work of Bird, Stewart and Lightfoot. Additionally the treatment of chemical reactor systems mathematically by Aris and Amundson was resulting in widespread acceptance of this profession [6]. The application of these chemical engineering concepts to the agricultural engineering discipline led to many improvements in the production of food and its subsequent processing. While chemical engineering paved the way for quality of life improvements made by new plastics, fuels, polymers and other synthetics from petroleum, agricultural engineering remained more focused on raw materials that were renewable and living. The renewable materials were generally more heterogeneous, less stable, perishable, and created microbiological issues, leading to less support compared to the synthetic alternatives. However, they remained critical to fulfilling needs that synthetics could not, particularly food, feed, and fiber. The comparable advantage of synthetics led to a resurgence in better defining the agricultural engineer. At the 1960 winter ASAE meeting in Memphis, G. W. Giles explained his vision for the role of the agricultural engineer, alluding to 'the internal mechanism of biological production and to the external operation and environment that influence this mechanism.' He stated, 'Some may say that the science of biological processes should be left to the pure scientist and that agricultural engineering should confine its activities strictly to engineering practices. Regardless of whether it is called pure science or not, the fact remains that the mathematical relationships of the physical to the biological processes are basic to developing superior engineering systems. Our profession needs some fundamental (phenomenological) law(s) upon which to base our (technical) judgments and guide our direction and pattern of growth for engineering the biological system. The core of our profession should be built on engineering laws governing the intricate complex processes of plants and animals. This is the thing that distinguishes agricultural engineering from other engineering professions.' According to Loewer [7], ASAE and higher academic institutions supported this notion—even leading to changes in some of the agricultural engineering curriculum names—but the primary audience at the convention hearing Giles' speech, being industrially based, was less inclined toward the movement.

More recently, in 1987, agricultural engineering departments began to re-emphasize these ideals at a conference entitled 'Project 2001—Engineering for the 21st Century,' resulting in development of several workshops to better shape the future direction of the undergraduate curriculum. Of note were the two primary conclusions about the core definition of the discipline:

1. The core curriculum for our undergraduate engineering program should be based on the biological sciences to the extent that our graduates will be proficient in the engineering aspects associated with quantitative biology.
2. The core curriculum should significantly expand the capabilities of our graduates to effectively address the changing needs of society for engineering related to biological systems.

Within the last two decades, consumers have increasingly placed more stringent requirements on agriculturally derived product quality and convenience, as well as having greater sensitivity to environmental issues. As non-renewable petrochemical resources become less available, consumer pressure for equivalent/superior products from renewable resources will continue to grow. These demands have created tremendous challenges for the agricultural engineer. With the emergence of new biotechnologies, Agricultural Engineering is uniquely positioned among the engineering disciplines to play a pivotal role in the evolution of Biological Engineering.

DEFINING BIOLOGICAL ENGINEERING

The common bases for all engineering disciplines are science, mathematics and economics. We will focus on the distinction conferred primarily by the first two core fields. The quantitative modeling of natural phenomena, combined with Terrullian's *novum extraneum ingenium* to meet social or political needs, defines the significance of engineering. In this respect, biological engineering is no different than any other engineering discipline. Differentiation between the various fields comes from the set of scientific principles that are used and what sociological needs are addressed. For example, some of the inherent differences between chemical engineering and mechanical engineering are found in differing emphases on statics/dynamics and mechanical properties of materials versus chemical reaction kinetics, rheology, unit operations, and vapor-liquid equilibria. Alternatively, industrial engineering places a strong emphasis on modeling of coordinated manufacturing operations and interactions with human operators to meet sociological/economic needs.

Clearly defined concepts in biological systems (i.e. ability to reproduce, autonomous behavioral nature, and self-maintenance, etc.) delineate the life sciences from purely physically based branches of science. Although mechanistic principles from other sciences, such as physics or chemistry, have been applied to model biological systems, far fewer specific quantitative principles have been uniquely defined for living systems to date. For example, Newton's Laws of Motion, Ohm's Law for electrical phenomena, or the Laws of Thermodynamics all represent fundamental laws in the fields of physics and chemistry. While biological systems, viewed as physical systems, must also obey these constraints, the development of quantitative laws distinguishing biological systems is comparatively in its infancy. Biology is predominantly still a descriptive, taxonomic science, based on somewhat arbitrary classification criteria (e.g. phenotype similarities, histology, DNA sequence homology, etc.). Some mechanistic principles are well-recognized, such as the helical, double stranded nature of DNA with 1:1 pairing of the four nucleotides and Central Dogma (DNA → RNA → protein). However, basic quantitative laws upon which to distinguish and engineer living systems do not yet exist. In part, this is due to the lack of a clear definition of what differentiates a living system from inanimate physical systems.

More than a century ago, Louis Pasteur, the father of modern microbiology, addressed this issue by asking two related questions:

1. Can biological chemical structures be produced from non-living precursors?
2. Can a living cell/system be created from only non-living components?

The first question was effectively answered by Fredrich Wohler in 1828 with the synthesis of urea. Since then, numerous equivalent examples ranging from basic Fisher-Killiani carbohydrate syntheses to complex protein and DNA chemical syntheses have been reported. The answer to the second question, however, remains unanswered. Over the past several decades, several researchers have initiated studies to address this question. In the mid-1960s Arthur Kornberg, known originally for the discovery of DNA polymerase, worked to induce replication of an entire viral genome and was successful with the addition of a DNA ligase unveiled by Lehman and Gilbert independently in 1967 [8]. The media's proclamation that he had created life in a test tube would seem a bit premature, as the system was not independently living, requiring a virus, and did not sustain its own existence. Nonetheless this work was a marvelous breakthrough at the time and the creation of biologically active molecules has since become rudimentary for those in the field. Still, whether creation via virus or even using PCR techniques, biologically active molecules alone are not the definition of life. They alone are not self-generating nor can they perform autonomous self-maintenance. More recently, other researchers have started to explore membrane-based, self-assembling systems which appear to have very limited autonomous replication properties [9–11]. However, these authors recognize that, even with current capabilities to isolate/synthesize the components of a living cell, simple combinations of these components does not create a living system.

The distinction conferred upon the study of living systems advocated here is not a belief in vitalism—the thought that physicochemical processes cannot explain living processes—but rather that the chemistry and physics of living systems, while familiar and explainable, at the micro level result in complex structures that have unique properties with their own definitive nature.

Let us consider further the example of proteins. It is generally accepted that protein structural homology is more highly conserved than sequence homology. The chemical compositions that allow proteins to fold explain the formation of these structures, but why different sequences exist for the same structure and function involves evolutionary selection and possibly some probability. It is the combination of chemistry with other physical factors to create patterns in biology, many of which remain unexplained due to their complexity, that distinguishes biological systems and therefore relegates it and its engineering to unique study.

Through mathematically descriptive models of phenomena, consistent fundamental principles used in engineering design are created. Hence the discipline of biological engineering awaits further elucidation of these laws before claiming true disciplinary uniqueness. It is likely that the hindered discovery that these 'biological laws' are at least partially a result of very small-size scales, the complexity of living systems, and the qualitative nature of historical biology (i.e. over-dependence on taxonomic descriptors) that has created animosity towards mathematics in researchers in the field. Recent scientific advancements in genetics, bioinformatics, and access to micro- and nanoscale measurement techniques have led to intense research and rapid development in our understanding of biosystems and will advance engineering systems in biology.

Although this understanding is still limited, we can examine conceptual inherent differences between living systems vs. non-living phenomena, remembering that the fundamental mechanistic scientific foundations must be consistent (e.g. laws of thermodynamics, fluid dynamics, chemistry, etc.). We propose four key differences that distinguish the engineering of living systems from non-living systems:

1. Living systems exist at cyclic, steady-state conditions far from thermodynamic equilibrium, for example metabolic cycles (e.g. TCA cycle).
2. Living systems spontaneously export entropy to maintain internal structural organization, stability, and growth. This can be seen in the ability to adapt to changing external conditions to maintain internal stability (e.g. digestion/excretion and perspiration).
3. Living systems are inherently self-reproducing. The need and capability to reproduce is instinctive in all living systems, from single-cell structures to the most complex mammals (e.g. mitosis, meiosis, and sporulation), though it is not necessarily advantageous to the parent.
4. Living systems possess inherent, self-adaptable affinities for other living systems (or inorganic systems) at all levels, ranging from the molecular to the whole organism. Examples of this idea include: antibodies, enzymes, protein

synthesis/folding, intercellular microbial attraction, pets, children, mates. Orchestrating the structural complexity of even the simplest single-cell organism is still only possible through the mediation of a living organism.

Modeling highly complex, compartmentalized mixtures of synthetic or even biological macromolecules/components and quantifying their entropic content during steady state alone is a formidable challenge. Adding the kinetics of self-assembly, energetic initiation, and self-reproduction is equally daunting. On top of this, our inability to control/initiate/model highly non-equilibrium thermodynamic systems makes the task of building living systems *de novo* well beyond our current capabilities. Conceptually, this bears similarity to questions in physics related to the initial state of the Big Bang theory or to current philosophical issues regarding evolution and creation theories.

Similarly, developing quantitative descriptions of these principles is highly challenging. Relatively simple molecular binding/attraction models have been developed (e.g. the Michealis-Menten kinetic reaction equation). However, given the complexity of highly regulated, interconnected, multiphase, multicomponent living systems, it is likely that novel forms of mathematical description may be needed. Put in a more prosaic form, how do you mathematically quantify love?

While future advances in molecular biological techniques and methods will provide new tools to researchers, the accomplishment of this goal will require significant advances in the field of non-equilibrium thermodynamics and the understanding of how living systems develop templates/patterns which are used to initiate new living systems. Developing these advances will likely require the formation of new concepts and laws of how living systems work, which will be the basis of Biological Engineering. Hence, Pasteur's second challenge may be the technological starting-point for Biological Engineering.

BIOLOGY AND ENGINEERING: THE NAME GAME

With recent advances in and social impacts of the life sciences, many engineering disciplines are rushing to change their names to capture public attention by incorporating some aspect of biology in their names. Disciplinary names abound, including bioengineering, biosystems engineering, biochemical engineering, biomolecular engineering, biomedical engineering, bioresource engineering, and others. Each has a slightly different applications focus, usually incorporating traditional engineering disciplinary principles with some aspect of a living system. Civil engineers, for example, often work with waste treatment bioremediation. Electrical/computer engineers are developing hybrid electronic/living system interfaces and sensors. Chemical engineers are known for their expertise with fermentations, and agricultural engineers with food/bioprocessing Biomedical engineering focuses on both physical and energetic interfaces between physical engineered systems and human living systems, exploring the biological responses to the implantation/application of the physical systems. Novel advances in micro- and nanotechnologies with electrical/mechanical systems provide the opportunity to work at cellular and molecular size scales.

This diversity of examples contains a common theme: they are focused on developing externally engineered systems/environments that interact with a living system to alter its behavior/properties. A more fundamental definition of biological engineering would focus on altering existing internal biological processes which control physical attributes/behaviors.

The distinction for biological engineering stems from what is being altered. Changing the environment (external) to the living matter is not biological engineering by our definition. Changing the inherent, self-perpetuating identity of living matter itself (internal) is the definition of biological engineering. Our belief is that biological engineering should fundamentally require more than just the application of external stimuli to living systems to affect how they act. Rather it should involve the changing of the biological system itself, invoking a controllable change that becomes a self-sustaining, integral part of the identity of the living system. For example, a heart pacemaker does not affect the identity of a person but provides a consistent external stimulus that causes the heart tissue to act in a controlled fashion. We would define this as an example of biomedical engineering, but not biological engineering. Another example is the use of immobilized enzymes to produce DNA sensor chips. This application of biotechnology uses electronic engineering principles associated with a component of a living system (antibodies, proteins), but it does not intrinsically change biological systems. Hence this would not be an example of fundamental biological engineering by our definition. On the other hand, the controlled genetic alteration of a metabolic pathway within an organism that causes it to overproduce a chemical intermediate is an example of biological engineering, because this change becomes an integral part of the system, carried over in the reproduction of the living cells to alter inherent behaviors.

THE EVOLVING ROLE OF AGRICULTURAL ENGINEERS AS BIOLOGICAL ENGINEERS

Arguably, foundations of the historical Agricultural Engineering discipline have evolved to make it closely oriented to the new discipline of Biological Engineering. The broad base of engineering principles from many different disciplines combined with the focus on 'engineering biology' as the basis for the discipline make it distinctive from other physically based engineering disciplines. As G. W. Giles noted nearly half a century ago: 'The core of our profession should be built on engineering laws governing the intricate complex processes of plants and animals.'

Based upon the understanding that many different types of engineers will play a role in creating this discipline, what is the most logical role for agriculturally based biological engineers? Certainly one of the most promising areas is that of plant-based biological engineering for bioproduction. Having worked with plants for production of food, from the beginning of the profession, through dependence of plant breeding, irrigation and soils, growth, pest and herbicide management, through to harvest and post-harvesting, the background of the agricultural engineer is clearly well suited to developing plants as production systems for novel compounds through biological engineering. This incorporates a host of application demands, such as the renewable production of fuels, chemicals, foods, and nutriceuticals, and thus these topics of study would seem to be the most logical areas whereby traditional agricultural engineers could benefit society.

CURRICULAR ISSUES IN BIOLOGICAL ENGINEERING EDUCATION

The ability to quantitatively measure and model life processes is rapidly moving qualitative biology toward becoming a basis for engineering design and innovation [12, 13]. This growth has highlighted the need for highly interdisciplinary educational methods, from both the science and engineering perspectives. Building an integrated educational curriculum in BE will require categorizing basic engineering and biological science concepts, facts, and examples in a way that demonstrates their inherent relationships. This task must entail more than a curriculum redesign that simply shuffles existing courses in different departments. It will require a high level of collaboration between current faculties from a variety of disciplines, embracing the idea of comprehensive, interdisciplinary education. The willingness to operate in a 'give and take' environment to identify key concepts and examples without dogmatic insistence along traditional disciplinary educational lines will be critical. For example, finding ways to merge key concepts in biology, physics, and chemistry into thermodynamics or reaction kinetics courses that meet engineering modeling imperatives is needed. This will require the redesign of current disciplinary courses to become courses in engineering biophysics or biochemistry. This process will require substantial collaborative efforts among faculty and departmental administrations, which will be an evolutionary process.

In addition to technical skills, Biological Engineering must emphasize critical thinking, communications, professional responsibility, and interpersonal skills. Within the last several decades, society has placed increased demands on product quality, safety, and convenience. The consumer is more sensitive to environmental and safety issues as well. As non-renewable resources continue to diminish, societal demands for equivalent products from renewables will be greater than ever. The abilities to produce and process large quantities of raw and processed feed stocks to replace petrochemicals will require a combination of backgrounds in chemistry, biology, agriculture, and economics. These issues not only create tremendous challenges for the biological engineer in the areas of food and pharmaceutical and industrial bioprocessing, but also highlight the increased visibility of biological engineers in everyday consumer societal needs. This visibility carries both important benefits and responsibilities that fall on the shoulders of biological engineers. In addition to a high level of technical skills, biological engineers must also be able to effectively communicate the potential impacts and risks of their discipline in public and political arenas. Examples are the development of genetically altered plants or animals for food or industrial products or the development of sophisticated micro/nanoscale living biosensors. The potential impacts of these on intimate everyday human activities in food and medicine are staggering, both economically and socially. The ability of the biological engineer to evaluate, recognize, and inform society of the risks and benefits of these technologies is an important part of the educational process.

An example of a currently evolving Biological Engineering curriculum to address these issues is Purdue's Biological and Food Processing Program, which can be found at https://engineering.purdue.edu/ABE/Undergrad/fpe.whtml.

CONCLUSIONS

Today the historical convergence of advances in biology and societal needs for renewable sources of energy and industrial materials, human/animal welfare, and new materials have created an exciting environment for the creation of a new engineering discipline based on biology. While current engineering disciplines will expand to incorporate features of the life sciences, the opportunity exists for a new discipline, Biological Engineering. The identity of Biological Engineering should be based on establishing fundamental engineering/scientific principles based on concepts that uniquely distinguish living systems, as well as understanding their relationship to the existing physical sciences and engineering principles. While historical evolution from Agricultural Engineering to Biological Engineering exists, development of new curricular models and integrated topical structures are needed to educate biological engineering students and create a clear, distinct identity for graduates.

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