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Bringing life to engineering: biological engineering at the graduate level

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Biological engineering will be important for the future application of advances in biology to solve problems facing humankind. The philosophical foundation for broad undergraduate biological engineering programmes has previously been given, but biological engineering graduate programmes, where specialization normally occurs, have remained undefined. While specialization will continue in these graduate programmes, efforts must be made to relate research and teaching results to: (1) the analogical systems approach; and (2) the derivation of biological information to produce new general engineering techniques. Finally, a set of graduate-level core courses is suggested.

1. Introduction

Biology will define scientific progress in the 21st century, with the consequent key challenge to the engineering profession being how to respond to the biological revolution to achieve the potential that exists (Nerem 1997). That challenge can be met in a number of ways. The authors hope that presentation of this approach will act as a catalyst for healthy discussion of curricular approaches in this rapidly growing field.

One approach is to develop curricula based on a segment of the overall discipline (e.g. biomedical engineering develops from medicine or biochemical engineering develops from chemical engineering). Strong financial support from the Whitaker Foundation in the USA has fostered educational programmes in bioengineering with medical emphases. Faculties in these programmes, however, are still struggling with consensus to define objectives and content of both graduate and undergraduate academic programmes (Linehan and Harris 2000). Because the pool of funding for biomedical research keeps growing, engineers from other academic disciplines besides bioengineering are also taking advantage of new opportunities to work with biological systems (Green 1999). While curricula based on focused approaches are at various levels of maturity, many academic programmes in bio-based engineering are trying to find answers to questions of identity, philosophical bases, core course requirements and other issues that help to define the bioengineering field as unique.

The Institute for Biological Engineering (IBE 2002) defines biological engineering as ‘the biology-based engineering discipline that integrates life sciences with engineering in the advancement and application of fundamental concepts of biological systems from the molecular to ecosystems levels’. There are presently a number of groups attempting to

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define biological engineering more narrowly, but it is this broad definition that poses both the full promise of engineering interacting with biology and also its most pressing challenges.

Thus, an alternative curricular approach treats biological engineering as a discipline based on the broad science of biology. This paper supports a broad-based approach to biological engineering, which has been described (Johnson and Phillips 1995) as a broad and fundamental discipline in which engineering interrelates with biology. Unlike the bioengineering vision fostered by the Whitaker Foundation, biological engineering includes not only medical applications, but also applications in agriculture, biotechnology, ecology, food and others wherever biological systems are found. This field can be made truly unique, because it is a science-based engineering discipline based on biology and not tied to any particular applications area.

The new discipline of biological engineering was described by Johnson and Philips (1995). The emphasis in the paper by Johnson and Phillips was undergraduate biological engineering education. The undergraduate curriculum in biological engineering has been structured in a fashion similar to that used in other engineering disciplines. During the first phase at the University of Maryland, students receive a foundation in science and mathematics, including calculus, chemistry, physics and, especially, biology. In addition, they receive a strong foundation in engineering. The engineering courses include statistics, dynamics, strengths of materials, thermodynamics, electrical circuits, fluids, etc. Because the courses in the first phase are taught by discipline specialists, students develop an appreciation for the abilities of the different disciplines, as well as the necessary ability to function in a multidiscipline environment.

During the second phase of their curriculum, the emphasis is placed on integration of biology and engineering. For example, materials science and engineering is applied to living tissues and bone in a course entitled `Biological Materials'. Process engineering is applied to biological systems in Biological Process Engineering and controls theory is applied to living systems in Biological Systems Controls.

In the third phase of the curriculum, the undergraduate students acquire the specialized skills necessary to function in specific industries, such as biomedical engineering, bioenvironmental engineering, biotechnology, and ecological engineering. These skills are acquired through a combination of two advanced biology courses and four focused engineering courses. It was envisioned that graduates of biological engineering programmes could expect to be able to find employment with Bachelor's degrees. However, as with all engineering disciplines, additional education in their chosen specialty along with continuing education would be required as part of becoming and remaining competent in their job demands. Some of this additional education could come about through on-the-job training and continuing education; in other instances graduate school would be required.

There is a question whether this broad and fundamental approach could be maintained at the graduate level, where the tendency is to focus more narrowly on specific topics of study and research. Certainly, in the development of a new discipline, especially one derived evolutionarily from older disciplines, the tendency is to retreat to more familiar graduate patterns. Thus, we find graduate programmes in biological engineering struggling with a need to develop a unified approach. Faculty and graduate students with research interests in such areas as bioenvironment, bioprocessing, bioinstrumentation, biosensors and physiological modelling have thus far tended to retreat to these applications areas. Yet, these faculties often find themselves together in a biological engineering programme, and with seemingly little in common. Teaching at the undergraduate level is easier for a broad and fundamental biological engineering, because the teaching is not defined by the applications areas as it often is at the graduate level. So what should be the unifying concept for graduate programmes in biological engineering?

There is a need for dialogue and coalescence to a general understanding of what it means to be a biological engineer, what should define biological engineering research and what common knowledge can be expected from biological engineers no matter what specific applications or research areas they are interested in. There are similar definitional problems associated with other engineering disciplines, especially in these times of multidisciplinary collaboration, but the problem is especially acute with a new engineering discipline.

Views in this paper are the result of (1) conversations with representative faculty in bioengineering and biological engineering; (2) authors' experiences with studying and teaching bioengineering subjects to students for over four decades; and (3) the need to refine the graduate biological engineering curriculum at the University of Maryland. The authors do not suggest that the views presented here are the consensus of all faculties and programmes in biological engineering, nor do they intend these views to be completely applicable to bioengineering programmes that exclude non-medical applications. Instead, this report presents one approach to the very difficult problem of defining a new discipline at the graduate level.

2. Systems approach

Graduate faculties in biological engineering who maintain their identities defined by the application areas embodied by their research have very little in common with fellow faculty members with very different research foci. If biological engineering is to achieve a disciplinary identity, it must overcome this tendency for fragmentation. Forging coherent biological engineering graduate programmes will require reframing of research topics with a new perspective. Specifically, we must identify the core attributes of a biological engineer before we move on to specialization.

One of the common attributes of a biological engineering graduate programme should be a systems approach to engineering problems involving the life sciences. That is, biological engineering research should teach students how to manipulate living systems for the betterment of humankind. The emphasis should be on integrating the many influences characterizing biological problems to form coherent analyses that are worthy of the complex nature of these problems. It is a characteristic of biological processes that they must be examined as systems, because localized changes often result in system-wide effects. In the years since the publication of the Johnson and Phillips paper, many more biological engineering programmes have been established, for a total of *23* in 1997 (ASAE 1997). Eleven of these programmes are called Biological Systems or Biosystems Engineering in recognition that a systems approach is essential to biological engineering.

Life science research has tended toward the reductionism of focusing on smaller and more fundamental issues. Biomedical engineering, bioprocess engineering and others have often followed this trend, so we find the subspecialties of tissue engineering and metabolic engineering, among others, describing engineers who have focused on the cellular or subcellular level.

That reductionism is useful, because it feeds the revolution going on today in biological knowledge. We need to know more and more about smaller and smaller issues because the foundations of biological essences are found at the subcellular level. However, engineering application of this science requires that we work with the entire organism or collection of organisms. Thus, biological engineering graduate programmes should be able to maintain a systems perspective in their research and teaching. The systems perspective provides the unification tying bioenvironmentalists with biomedical specialists.

Part of this philosophy is embodied by the physiome project advocated by Bassingthwaite (1998). The physiome has been proposed as a means to explain or predict phenotypical attributes of an organism through physiological models that begin with genetic sequences. While such a model would need to be systems oriented, a full systems approach would require that environmental effects, usually considered to be as important as genetic factors, be accounted for. The model would probably then begin as rather shallow, but broad. As with many physiological models, 80-90% of the set of final results can be obtained with the simplest of assumptions; the last 10-20% requires a great deal of complexity. A systems analyst familiar with biology would realize that effort on more complex versions of a physiome model would be limited by the law of diminishing returns in the context of natural biological variation.

Equally important to the development of this process is the development of a coherent system for describing the connections and interactions between the elements of the system. A biological equivalent to the circuit diagrams used in electrical engineering or the bond graphs used in mechanical engineering must be developed. The development of a system for describing complex biological networks is further complicated by the difficulty in identifying the behaviour of the discrete components. Historically, engineering elements have been designed to behave in a consistent fashion. For example, resisters are designed to have nearly the same resistance throughout the entire range of their expected operating conditions. This is not the case with living materials. They are often extremely non-linear in their behaviour. Analysis of biological systems is further complicated by the fact that they not only respond to their environment, but also alter their environment. Furthermore, the biotic components of the system respond and adapt to each other.

A systems approach is not necessarily unique to any field of engineering, but for a coherent biological engineering to emerge, the systems approach is essential (Schreuders and Johnson 1999; Johnson and Schreuders 1999). By emphasizing systems: (1) we hope that a few general principles emerge to replace the many individual facts related to various biological systems; (2) the opportunities to apply biological engineering knowledge to new applications might become apparent; and (3) faculty and researchers should remain cognizant of the place where their works fit into the overall scheme of biological engineering epistemology.

3. Biology applied to engineering

A second basic attribute of biological engineering graduate programmes should be the ability to formulate new engineering approaches using information gained from biological systems. That is a difference between undergraduate and graduate programmes: undergraduate education should achieve a goal of familiarizing students with the application of engineering to biological systems, or, in other words, bring engineering to life. Graduate education and research should also attempt to discern from biological systems new engineering approaches that can be used for applications that may not include biological systems. In other words, graduate research should try to bring life to engineering.

Bringing life to engineering is related to, but different from, bionics and biomimetics. Bionics (presently called hybrid systems) can be defined as augmenting or replacing operations and functions of human extremities through machinery controlled by human neural systems (Bionics Symposium 1960). Bionics has also come to mean the application of knowledge of living organisms to the solution of engineering problems. The essential aspect of bionics was, at least at one time, considered by the military for advanced weaponry that combined the strengths of artificial mechanical systems with those of living human or animal brains.

Biomimetics emphasizes the imitation of biological material or functions in the construction of artificial devices or systems. Thus, biomimetics is the term applied to imitation of dolphin sonar to identify undersea objects and to the formulation of new materials constructed to be similar to those in biological organisms.

The emphasis in both of these approaches is to apply knowledge of biological organisms to solve engineering problems not necessarily involving some aspect of biology. Biological engineering research and instruction at the graduate level should do this and more; it can add modelling to basic scientific biological observation to form a design tool for problem solution.

An example of a research programme with a goal of extracting the essence of biological information to modify engineering design of inanimate objects comes in the design of air-purifying respirator masks (Johnson and Dooly 1995a,b). The reason for the existence of these devices is protection of wearers against airborne contaminants, yet sometimes severe performance decrements accompany respirator use. Are there ways to change configurations of the masks to minimize performance decrements? Information obtained from physiological modelling and laboratory experimentation has begun to indicate that the answer to this question can be affirmative. This research programme is typical of equipment or devices that can be appreciated by other biological engineering faculty.

Another significant potential exists in developing an understanding of the relationships between complexity, self-organization and stability. These attributes are commonly encountered in ecological systems (Capra 1996). The use of large numbers of similar elements to create complex, yet stable, systems is common in nature (e.g. trees in a forest, ants in a colony, or neurons in the brain). These concepts have been successfully transferred to computer science and engineering in such techniques as neural networks and genetic algorithms (Bentley 2001). As engineering projects, such as the Space Shuttle or the Internet, become increasingly complex, biological systems may provide a template for successful engineered systems.

4. Challenges of the teaching programme

To be able to become familiar with the vast amounts of knowledge required to integrate the many details of large numbers of specific life processes into a systems approach is not an easy task. Sometimes the essence of a biological problem can be adequately modelled without including minute details of the processes involved. Often, however, desired realism is not achieved without including vast numbers of details. Some means is necessary in order to economize on the amount of information that must be learned.

One means to do this is the analogical systems approach (Johnson and Schreuders 1999; Johnson 1999), where similarities among disparate biological systems are emphasized in order to describe the general nature of biological system behaviour. That way, general expectations about biological system behaviour can be formed in an economical way. Much needs to be done to catalogue general behaviours and notable exceptions in order to classify biological information for the engineer to use. The promise of successful description of complex systems using simple elements and rules has been supported by the complex behaviours exhibited by cellular automata programmed with very simple rules and by the successful application of Lindemayer's System to describe the structures of plants (Bentley 2001). However, no successful attempts at global categorization have been made.

Two parallel examples come to mind. First, the periodic table of the elements accomplished a similar goal for the field of chemistry; biological engineers need a periodic table of biology. Dmitrii Mendeleev formulated his periodic law of chemical properties in 1869 as a teaching aid, but the pedagogical value of the periodic table was recognized very quickly (Brush 1996). Not only was the periodic table able to add a general order to the many individual pieces of information known about chemical elements, but the table was also used as a blueprint to correct misinformation about the atomic weights of beryllium, yttrium, cerium, uranium and tellurium. In addition to these retrospective successes, Mendeleev used the periodic table to predict the discovery and physical properties of gallium, scandium and germanium.

The successful adoption of the hypothesis represented by the periodic table probably depended more on its prospective predictions rather than its retrospective classifications (Brush 1996). An analogous classification scheme for information about biological systems may not be as useful for prediction as it is for the ordering of known information, but, if myriad pieces of individual facts could be replaced by a few general principles, then the scheme would be extremely useful nevertheless.

It might be argued that a classification system for biological data analogous to the chemical periodic table could not be successful. There are too many possible exceptions to any general rule providing structure to the realm of biological system information. However, as Scerri (1997) points out, the periodic table is only approximate, and does not represent a perfect relationship between periodic behaviour and atomic structure. Moreover, identification of the anomalies in the periodic table serves as motivation for further work in the field of chemistry. One can imagine, therefore, a classification scheme for biological characteristics that proposes to order at least the most general biological properties, and that this scheme should be subject to revision as experimental, conceptual and theoretical research results become known. Graduate-level biological engineers would seem to be appropriate people to carry on this work.

Functional genomics, or the correlation of resulting function with genetic material, will not be able to serve as the needed ordering scheme, at least for the foreseeable future. When comparing similarities between biological systems at the cellular and ecological scales, one might be able to ascribe functions to the underlying genetic code better for a cell than for the higher ecological level. Yet, there are similarities at these disparate biological levels that could be understood better if an ordering scheme were available for presentation to students.

The second possible means of simplification of biological information involves dimensionless numbers. Heat transfer research results were made much more general, and thus more economical to learn and use, by the use of dimensionless numbers (McAdams 1954). Biological engineers need to find biologically relevant dimensionless groups to unify biological engineering knowledge and reduce the number of facts to be learned. Both of these projects can keep biological engineers busy for many years.

Use of dimensionless numbers for biological systems is still quite rare, but beneficial when used. DiMilla *et al.* (1991) used dimensionless numbers for such parameters as cell length and width, cell surface receptor densities, cell-substratum adhesiveness, cell speed, endocytosis rates, and others, in a model to predict migration characteristics of mammalian blood and tissue cells. On a different biological level, Johnson *et al.* (1992) used a dimensionless formulation of human performance data to eliminate all influences other than the respirator masks that were the objects of study.

Dimensional analysis was used to produce design equations for acoustical systems (Murphy 1950), which was one of the earliest applications of dimensionless numbers to a problem of biological nature. Before then, dimensionless numbers, especially the Reynolds number, were used with flowing water systems. These same techniques are still used by bioenvironmental engineers dealing with flowing water or air, but these applications cannot be said to be strictly biological.

5. Suggested core courses

There are, of course, different courses that will be required by graduate students with specialized interests in biological engineering. Speciality topic courses are necessary to give students the knowledge bases to perform their research and to function effectively in the work environment after they graduate. General topic, or core, courses are also necessary to define the biological engineering field and to give graduate students a common core of information and approaches that they can use to understand each other. The information content of these courses should enhance the abilities of biological engineers to connect engineering and the biological sciences in unorthodox ways.

A thorough knowledge of the life sciences is required for biological engineers. Johnson and Phillips (1995) discussed life sciences courses at the undergraduate level. The functions of these courses were not only to teach students knowledge about biological systems, but also to expose the students to the problem-solving approaches used by life scientists, which are at times more appropriate than techniques used by engineers. For students who study biological engineering at the undergraduate level and who continue their studies at the graduate level, there should be a strong foundation upon which to build advanced biological techniques. Those students should be required to take appropriate advanced life sciences courses. For those students who did not study biological engineering at the undergraduate level, remedial life sciences courses might need to be taken before advanced courses. It is not realistic to expect graduate students to do well in advanced life sciences courses without adequate preparation. Modern biological sciences are much too sophisticated to treat the field cavalierly. Thus, courses such as biochemistry, microbiology, molecular biology, genetics, physiology, ecology and other appropriate courses should be taught by specialists in those areas.

While the content of biological engineering course work will continue to evolve, the diversity of biological systems suggests that the core curriculum should be based on the development of a student's ability to: (1) acquire information about, (2) describe and (3) manipulate and predict the behaviour of living systems. Furthermore, because of the need for specialization courses, the decision to add core courses must be approached with parsimony, building upon the recommendations in the report of undergraduate biological engineering core courses (Garrett *et al*. 1992). We would suggest the following courses.

Development of an ability to acquire and understand biological data

(a) *Measurement Systems.* The operation of measurement is extremely important in biological engineering (Shuler 1998). Rather than focus on current instrumentation technologies, this course should be concerned with the generation of measurement information, including transduction and energy exchange, manipulation and presentation. Graduate students should be prepared not only to use instruments to measure biological phenomena, but also to develop new measurement methods when appropriate.

(b) *Biostatistics.* Biological data are inherently noisy. Unlike graduates of many engineering disciplines, biological engineers must be comfortable with biological diversity and variability in response. Furthermore, they must be fluent in the statistical methods used to analyse and describe biological variation.

(c) *Bioinformatics.* This is the technology of information manipulation, and is important to biological engineers because of the vast amounts of information that are being gathered from biological organisms at various levels. The information presently coming from the various genomes being studied is of great magnitude (Shuler 1998). The creation of massive datasets in medicine and ecology is also occurring.

Development of an ability to describe mathematically the behaviour of living systems

(a) *Biological Systems Modelling.* Such a course should emphasize modelling approaches to capture the essence of a biological system (Whitaker Foundation 1998). This course should especially consider that biological systems reproduce and age, grow, change, respond to their environments and die. The course should explain the modelling steps of identification, reticulation, simplification, implementation, calibration, validation and revision as they relate to biological system description.

(b) *Transport Phenomena.* Transport processes taught at the graduate level should have a much more theoretical approach than the same processes taught at the undergraduate level. The processes included should be extended to information transfer and movement of biological entities (cells as well as organisms), both of which can be seen to obey the same basic equations formulated for heat and mass transfer.

Development of an ability to manipulate and predict the behaviour of living systems

(a) *Design Heuristics.* This course would include the methods of application of biology for the purpose of design (Wells 1998), and would be the means for showing students how life can be brought to engineering and engineering brought to life. One particularly fertile approach to this topic would be the use of case studies (Lauffenburger 1997, Poirier 1997).

Each of these courses should attempt to enhance imagination and independent thinking. Each should attempt to impose parsimony on the vast numbers of facts being generated to describe biological systems through the use of induction, analogy and database organization. Each should attempt to integrate approaches from biology, physics, mathematics, chemistry and engineering to produce a synthesized solution that goes beyond what each of these areas could achieve by itself.

It should be noted that these courses do not describe a complete graduate degree in biological engineering. These general courses are only a foundation for specialized courses, particularly in the area of design. The specific needs of work in each area require that the student will need appropriate courses in biology, biochemistry, engineering, or laboratory techniques. These focused courses are necessary for a graduate student to obtain true expertise in their chosen area of specialization.

In addition to these listed courses, graduate students are often required to present seminars on their research work. Again, the difficulty here is that graduate student research tends to be specialized and tends to obfuscate application to common biological engineering goals. A somewhat different approach to seminars might be in order: instead of treating a seminar as a local equivalent to a presentation given before a highly specialized technical conference, the emphasis of the seminar should be on those aspects of the graduate students' research that overlap the general field of biological engineering. Thus, the underlying theme of graduate student seminar presentations could be the contributions of their works to the general field of biological engineering. Just considering this question might position many more graduate students to be able to lead the field of biological engineering in the future.

6. Conclusion

The challenges to organize and construct biological engineering at the graduate level require imaginative approaches that move beyond research in speciality areas. To coalesce a biological engineering field from the various subdisciplines will require identification of common knowledge organized along general principles specific to the biological engineering discipline.

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