Biomaterials in Bioengineering Education:
Past, Present, and Future

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Summary

Bioengineers use materials. Materials are the stuff from which devices and organisms are made. The hard stuff, soft stuff, and even liquid stuff have a set of properties, characteristics, and principles. Bioengineers need to have some awareness and understanding of these subjects. Even if they are only involved in modeling and simulation, they must know the properties and characteristics of the tissues, organisms, and devices which they are attempting to model and simulate.

This discussion paper provides a brief historical perspective of the evolution of the field of Biomaterials. Classical and current educational materials are briefly reviewed, and preliminary recommendations for the near future are made.

The Past:

Biomaterials education has evolved together with the evolution of Bioengineering and Biomedical Engineering academic departments and programs.

In the late 50's and early 60's, with the development of a variety of new surgical techniques and interventions, there was a growing awareness of the need for materials with which to develop and construct a wide range of devices for implant and artificial internal organ applications. Although biomaterials had been widely used in the dental arena and for wound dressings, sutures, and various external devices and prostheses, implanted materials and devices were relatively rare until the late 50's.

As Bioengineering programs evolved, originally from Electrical Engineering/ instrumentation activities and Mechanical Engineering/biomechanics activities, there was an increasing realization of the need for these new bioengineers to have some background in the principles and tools of modern metallurgy, ceramics, and polymer materials.

Applications and activities in the area of artificial internal organs, especially internal cardiovascular repair, rapidly developed -- first vascular grafts, and later artificial heart valves and even ventricular assist devices and total artificial hearts. The practical development of hemodialysis also provided a strong interest in materials for membranes and tubing.These activities lead to a growing appreciation of the problems involved with the interactions between artificial materials and the vascular environment, particularly blood coagulation and thrombosis. The annual meetings and proceedings of the American Society for Artificial Internal Organs (ASAIO) contributed greatly to the development of these new areas and activities.

The development and widespread application of orthopedic implants, particularly the total artificial hip, led to a growing concern with corrosion and with the general biocompatibility of the materials used in orthopedic devices.

With the exception of the dental area, the field of biomaterials began with the adoption and application of materials designed, developed, and made available for other purposes. These commercial materials were employed as components of a wide range of medical devices.

Initially, most orthopedic implants used corrosion resistant 316 stainless steels. Later it was recognized that these materials did indeed corrode and released heavy metal constituents. The field began to adopt the more highly corrosion resistant but more difficult to fabricate cobalt (Co)-chromium (Cr)-molybdenum (Mo) and related alloys for orthopedic implant purposes. These materials, developed initially for the severe and hostile environment of jet turbine blades, were already being used for dental applications. Later, with the considerable development effort in the application of titanium alloys for aircraft and aerospace purposes, the lower density and very high corrosion resistance of titanium was recognized, and it was rapidly applied in orthopedics and other medical fields.

There was, therefore, an early recognition of the importance of the stability, biodegradation, and biocompatibility of materials for implant and related Bioengineering applications.

Ceramics received early recognition as being exceptionally stable, noncorrosive, potentially biocompatible, and even bioactive materials. It was also recognized that the mineral matrix of bone could be partially duplicated using in vitro ceramic material preparation processes. Activities and subfields focused on calcium phosphates, hydroxyapatites, and other bioactive ceramics rapidly developed.

It was realized early that ceramics and/or metals with various surface porosities and textures could influence bone ingrowth and adhesion, leading to an interest in processing, fabrication, and characterization technologies related to porosity and texture.

The polymer materials industry was already well developed in the mid 50's and has continued to grow. The initial polyester vascular grafts, prepared from commercially available fabrics for clothing, were soon augmented by a wide range of synthetic polymer materials, including polyethylene, polypropylene, polytetrafluoroethylenes (Teflons), new and novel polyesters, polyurethanes, and others. Each of these materials brought a unique set of properties as well as potential concerns.

Many new polymer materials were applied as suture materials, for example, polypropylenes, polyesters, and polytetrafluoroethylenes. There was considerable interest, investment, and success in the development of bioresorbable polymers, initially for sutures, including the polyglycolic and polylactic acids now used in tissue engineering.

The pharmaceutics and chemical engineering communuities applied the new polymer technologies, including novel membrane structures and hydrogels, to the challenge of the controlled and sustained delivery of drugs. The drug delivery community now has its own journals, meetings, and organizations (Controlled Release Society).

The novel properties of hydrogels and of other polymers, lead to the rapid development of contact lenses and other opthalmologic applications.

A seminal conference on Materials in Biomedical Engineering was organized and conducted by Sumner Levine in 1967 and published as an Annals of the New York Academy of Sciences in 1968 (Vol. 146 (1968) pages 1-359). That meeting served as a comprehensive, state of the art summary of the field of Biomaterials up to that time.

These growing activities, and others, led David Williams, a young graduate student completing his Ph.D. studies at the University of Liverpool, together with his orthopedic surgeon collaborator, Robert Roaf, to write and publish the first biomaterials textbook: Implants in Surgery (Saunders, 1973). The Table of Contents of the Williams and Roaf text is given as Table 1.

Table I: Contents of Williams and Roaf, 1973

Introduction to the use of implants
The structure of materials
The mechanical and physical properties of materials
The deterioration of materials in use
The response of the body environment to implants
The selection of implant materials
Implant production and design
Implants in orthopedic surgery
Implants in the cardiovascular and respiratory systems
Implants in plastic and reconstructive surgery
The current status and future development of implant surgery

That now classic book defined and established the subdiscipline of Biomaterials Science and Engineering. Several years before it was published the Journal of Biomedical Materials Research was founded and the Society for Biomaterials came into being. Both the Journal and the Society developed rapidly and have continued to grow.

There were biomaterials textbooks before Williams and Roaf.
Textbooks in Dental Materials have a long history – including publications of the American Dental Association. The Skinner and Phillips text on Dental Materials was already in its 6^{th} edition in 1969!

The Williams and Roaf textbook served as the basic structure and paradigm of the more general field of biomaterials for the next several decades. A number of additional textbooks evolved and enhanced the field during that time, including those by Park, Black, Hench, Bruck, Szycher and others in the 70s and 80s.
Additional topics were presented in these books, including blood compatibility, bioactive materials, tissue reactions, inflammation, protein adsorption, cell adhesion, complement activation, carbons as biomaterials, characterization and testing, sterilization, etc.

The Present:

Most major Bioengineering programs developed a curriculum which included materials, mechanics, instrumentation/electronics, and strong physiology/pathology/medicine components. It was expected that bioengineers, regardless of their particular undergraduate discipline, would develop some working knowledge of each of these areas, in addition to their particular specialization.

Although Bioengineering was primarily a graduate discipline in the 60’s and 70’s, undergraduate programs began to appear, develop, and expand in the 80’s and 90’s, usually including a biomaterials course or component, providing a growing market for new (and old) textbooks.

The concern with blood compatibility; tissue reaction; tissue compatibility; corrosion; and related biointeraction and biodegradation processes led to growing interest and emphasis on the surface chemistry, surface physics, and surface engineering of biomaterials used in medical implants. The rapidly developing and maturing fields of surface chemistry, surface modification, and surface characterization were applied to the new subdiscipline of biomaterials, resulting in means with which to engineer, modify, characterize, and apply surface and interface technologies to enhance the performance of biomaterials. This knowledge and potential is now reflected in recent biomaterials textbooks, including those by Silver, von Recum, and others, and in the later editions of the earlier texts.

Although the field of Biomaterials developed, expanded, and matured, the generation of textbooks, based in large part on the Williams and Roaf outline, did not fully respond to the new needs and expectations.

For example, several new subfields of Bioengineering and of Biomaterials Science and Engineering developed, including tissue engineering and the related field of biohybrid devices. Tissue engineering, following the earlier work on the endothelialization and tissue ingrowth of vascular grafts in the 60's, created a need for matrices with which to direct and support cell seeding, tissue growth, and development. The early experience with sutures and vascular grafts, and the technologies of bioresorbable polymers, fibers, and fabrics, are now being applied in tissue engineering.

Thus the Biomaterials Society, under the leadership of Buddy Ratner, designed, developed, and published what is perhaps the most widely used textbook today in graduate and undergraduate Bioengineering programs:

B. D. Ratner, A. S. Hoffman, F. J. Schoen, and J. E. Lemons, eds., *Biomaterials Science: An Introduction to Materials in Medicine*, Academic Press, 1996; ISBN 0-12-582460-2

The book is a state of the art (as of 1996) treatise with some 60 Chapters by experts in all areas of Biomaterials Science and Engineering. Although it is very comprehensive and current (a 2nd edition is in preparation), it is in many respects more of a resource and reference book than a textbook in the traditional sense; it does not have problems, laboratory exercises, or other educational aids (most of the earlier texts also lacked such resources).

Most Bioengineering programs today are in the process of including molecular biology and strong cell biology components in their curricula. There is growing interest in the design and development of new and novel materials using modern molecular biology methods. These new approaches are not yet well represented in the current generation of biomaterials text books.

The Whitaker Foundation’s Teaching Materials Program has recognized the need for textbooks in biomaterials for Bioengineering and Biomedical Engineering departments and programs, at both the undergraduate and graduate levels. A number of authors and author teams have expressed interest in the preparation and publication of such resources, and it is likely that additional and very different teaching materials for biomaterials education will become available in the near future.

During this period the world wide web/internet has come into being and provides a vast array of educational resources for modern biomaterials education and research.

The Future

Biomaterials education and materials for biomaterials education in modern Bioengineering programs, both at the undergraduate and graduate levels, will require a more thorough, comprehensive, and forward-looking treatment.

The bioengineers we educate and graduate today must practice in the world of tomorrow. The world of Bioengineering, and engineering and technology in general, is changing very rapidly. It is changing most rapidly in areas related to biology and biotechnology. The rapid developments in biology, including 30 fully sequenced genomes -- with an additional 60 to 70 in the next several years – and the availability of the generic human gene sequence -- means that much of what we now know and attempt to control in the areas of development, repair, regeneration, and medicine in general will change dramatically in the next several years.

Our students must be prepared to respond to this rapidly changing and exciting environment. They must not be too steeped and constrained by the knowledge of the past and even of the present. Although that knowledge is very important and provides a foundation, a basis, a structure, it should not provide unyielding boundary conditions and unnecessary constraints on their creativity, inventions, or future activities.

It is indeed likely that our dependence on man-made materials and devices for the partial repair of human disease and pathologies will become at least partially unnecessary in the years ahead. Biology, Medicine, and Bioengineering will learn to apply the information in the many new genomes to understand and then engineer the repair, regeneration, and even development of tissues and organs in ways which will largely minimize the need for artificial devices and constructs. The knowledge of biology and of the factors and processes which activate, enhance, augment, and control tissue repair and regeneration will move the field of Bioengineering from the engineering of artificial devices to the engineering of the repair and regeneration of tissues and organs. The subdiscipline of biomaterials will likely move from a dependence on artificial materials to the use of self-made materials.

Many will argue that it is simply impossible to provide the appropriate background in basic materials science and engineering, and the other topics which are now considered essential in traditional biomaterials courses and curricula, while at the same time including the appropriate concepts and tools of molecular biology, genetics, pharmacokinetics, pharmacodynamics, and related fields. Such tools, however, are likely to dominate biomaterials and Bioengineering, and indeed even materials science, in the years ahead.

The response to such an argument is simple: Given our improved understanding; given the computer, mathematics, and simulation tools and skills which are now available; and given the unique instruments and experimental tools which are now available -- including gradients, arrays, and other multivariate and multi dimensional means with which to observe, experience, and teach -- we should be able to effectively teach -- in a mere 3 to 7 years of a modern undergraduate and graduate Bioengineering education -- the knowledge and skills which perhaps took us 20, 30, or more years to develop and accumulate. That is indeed our educational and professional challenge.

Clearly the biomaterials course and curricular content employed in a specific department or program will be dependent on and synergistic with the other courses and activities in that program. For example, the University of Utah's new undergraduate Bioengineering curriculum includes a practical biochemistry experience in the freshman and sophomore courses; a biology and quantitative physiology exposure in the sophomore and junior years, and a strong biophysics/ physical chemistry component in the junior year. The senior year biomaterials core course thus builds extensively on that earlier derived knowledge and experience.

Bioengineering is a very diverse discipline, with many subdisciplines, tracks, and areas of emphasis. A core or basic biomaterials experience must be relevant to that broad and diverse population. Many of those students are unlikely to be involved with medical implants and may never need to deal with issues of blood and tissue compatibility. They may be involved in medical imaging; they may be involved in cardiovascular modeling and simulation; or in many other areas characteristic of modern, diverse Bioengineering programs.

In order to make biomaterials relevant to each Bioengineering student in a modern program, student-specific projects and/or research papers can be used in their courses. For example, the core biomaterials course at the University of Utah requires a research paper related to each student's specific area of research. Many topics which these students have developed are not normally included in current and traditional biomaterials textbooks. This requirement guarantees that each and every student appreciates the relevance of biomaterials to his/her specific area and interests.

A modern biomaterials course should include the traditional materials science and engineering background important to current practice -- but it must also include sufficient perspective and background on the near future developments which are likely to be applicable and relevant tomorrow. An outline of such a course –for discussion purposes-- is given in Table 2.

The selection of cases and applications will depend on the particular emphasis and interests of each specific department or program. Although it is not possible to cover all of the topics in a 1 or even 2 semester course, the basic materials can and should be fully covered by careful design and implementation of a synergistic, interactive set of courses and labs in the modern Bioengineering curriculum.

A list of textbooks, in chronological order, is also given.

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Table II. Topics for a Modern, near future Biomaterials Course: Man-made materials and the basic concepts of materials science (top) and bio-made or natural biomaterials (center) should be treated in parallel. The two areas should be compared and contrasted. The bottom list includes topics which are a synthesis or hybrid of both "synthetic" and "natural" processes and materials. The entries at the very bottom suggest other important areas, including going beyond today's Biology.

Man-made (traditional Materials Science)

Minerals to
Metals and
Semiconductors
Ceramics
Polymers and Block Copolymers
Additives and Impurities
Energy Intensive Materials
Environmental Stability
Environmental Diversity
Microstructure/Packing/Anisotropy
Processing and Fabrication
Properties and Characterization
- Physical
- Mechanical
- Chemical

Degradation Mechanisms
- Hydrolysis
- Corrosion

Bio-made Materials

CHNOPS
No Metals
Few Ceramics
Limited Environments
Turnover, Lifetimes, (in)stability
Cells/Matrix/Tissues
- Histology
- Materials Synthesis and Self-assembly
- Development and Specialization

Tissue Properties and Characterization
- Dielectric Properties
- Density
- Mechanical Behavior

Wound Healing, Repair, Regeneration
Pathology/Disease
Infection/Immune system
- Allergy
- Sensitivity

Individuality and Variability

Center:

Foreign Body Reaction
Microbes/Pathogens/Sterilization/Endotoxins
Biocompatibility
Wound Dressings
Tissue Engineering

- Bone
- Cartilage
- Muscle
- Soft tissue

Partial Implants
- Dental,
- Needles,
- Splints and Braces,
- Electrodes,
- Catheters,
- Biopsy devices
- Endoscopes

Blood and Blood Compatibility:
- Coagulation
- Thrombosis
- Complement

Case Studies and Applications (program and interest specific)

Sutures/Fasteners/Adhesives
Orthopedics
Cardiovascular
Neuroprostheses
Sensory Applications
Opthalmologic Applications
Dental
Renal/Kidney
Skin
Lung
Liver
Drug Delivery
Chemical Sensors
Physical Sensors
Electrodes for Stimulation
Cosmetic Applications
Medical Imaging
- Contrast agents
- Phantoms,

Modeling and Simulation
- Dielectric properties
- Densities
- Compliances
- Anisotropies

Model for Application Development:

Homework/Background
- Pathology/Medicine
- Mechanical Needs
- Chemical Needs
- Physical properties

Engineering

Model
Design
Materials selection
Prototype
Testing
Evaluation
Optimization
Retesting
Redesign
Reprototype

Testing and Validation
In vitro testing
Cell and tissue testing
Animal testing
Pre clinical testing

Issues related to Device Development and Application:

GLP and GMP
FDA
Animal testing
I R B, Clinical Testing
Ethical issues
Health Policy Issues
Reimbursement and other Economic Issues

Beyond Biology--the Farther Future:

Bio-hybrid Materials
Beyond t-RNA and Amino Acids
Beyond CHNOPS
Super materials
Teeth and bones: fluoride, etc.
Spider Silks
Enhanced bio-derived materials

References:

1966, American Dental Association, Guide to Dental Materials, 3rd ed.

1967, E. W. Skinner and R. W. Phillips, The Science of Dental Materials, Saunders, 6th edition,

1967, L. Vroman, Blood, Natural History Press

1968, S. N. Levine, ed., Materials in Biomedical Engineering, Annals New York Academy of Sciences 146 (1968) pages 1-359;

1971, R. W. Phillips, Elements of Dental Materials for dental hygienists and Assistants, Saunders,;

1973, D. F. Williams and R. Roaf, Implants in Surgery, Saunders,;

1974, S. Bruck, Blood Compatible Synthetic Polymers: An Introduction, Thomas,;

1975, J. H. Dumbleton and J. Black, An Introduction to Orthopedic Materials, Thomas

1979, J. B. Park, Biomaterials: An Introduction, Plenum Press

1981, D. F. Williams, ed., Fundamental Aspects of Biocompatibility, C R C Press

1982, L. L. Hench and E. C. Ethridge, Biomaterials: An Interfacial Approach, Academic Press

1982, D. F. Williams, ed., Biocompatibility and Clinical Practice, C R C Press

1983, M. Szycher, ed., Biocompatible Polymers, Metals, and Composites, Society of Plastics Engineers and Technomic Publishing

1986, D. F. Williams, ed., Techniques of Biocompatibility Testing, C R C Press

1992, J. B. Park and R. S. Lakes, Biomaterials: An Introduction, 2nd ed., Plenum Press,;

1992, J. Black, Biological Performance of Materials: Fundamentals of Biocompatibility, 2nd ed., Decker; 3rd ed, 1999.

1994, F. H. Silver, Biomaterials, Medical Devices and Tissue Engineering, Chapman and Hall

1996, B. D. Ratner, A. S. Hoffman, F. J. Schoen, and J. E. Lemons, eds., Biomaterials Science: An Introduction to Materials in Medicine, Academic Press,; ISBN 0-12-582460-2

1999, A. F. von Recum, ed., Handbook of Biomaterials Evaluation, 2nd edition, Taylor & Francis,; ISBN 1-56032-479-1

1999, F. H. Silver and D. L. Christiansen, Biomaterials Science and Biocompatibility, Springer,;