AC 2010-114: TEACHING OF BIOMEDICAL MANUFACTURING IN THE UNDERGRADUATE MANUFACTURING/MECHANICAL ENGINEERING PROGRAMS

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Biomedical Manufacturing in the Undergraduate Manufacturing/Mechanical Engineering Programs

Abstract

Biomedical manufacturing defined as "the applications of manufacturing technology to advance the safety, quality, cost, efficiency, and speed of healthcare service and research" is a rapidly growing field. This field is unlike many other businesses in the US manufacturing industry where downsizing is common in a slow economy. According to the US Department of Labor's Bureau of Labor Statistics, a 21 % employment growth can be expected for the biomedical engineers over the next decade. Only a few manufacturing programs offer biomedical engineering related courses. This paper describes the definition and characteristics of biomedical manufacturing. Topics (biomedical device manufacturing, biomedical product manufacturing, and surgical tool manufacturing) in biomedical manufacturing are also discussed. A survey of existing biomedical manufacturing related courses in the manufacturing engineering programs will be presented. The contents of these courses often contain an overview of anatomy, physiology, tissue and biomaterials, US FDA's good manufacturing practice, and medical device manufacturing.

1. Introduction

Manufacturing has changed drastically in the past years and the manufacturing engineering curricula has also changed. Recently, leaders in manufacturing education have been working on the recommended curricula, so called *Curricula 2015* [1]. According to the paper published in 2009 ASEE conference [1], bio-product manufacturing was chosen as a new discipline that the educators should focus on. For bio-product manufacturing or biomanufacturing, a unified definition is definitely lacking. Often, biomanufacturing deals with the production of pharmaceuticals and agricultural products [2], which is mainly a subject under the disciplines of chemistry, biochemistry, biology, and chemical engineering. The term, 'biomanufacturing', could be too broad and the manufacturing educators need to narrow down the scope. In 2008, Mechanical Engineering Professor A. J. Shih at University of Michigan published a paper on biomedical manufacturing [3], which has been studied actively in the manufacturing research community. In the same year, the special issue on biomedical manufacturing was published in the ASME Journal of Manufacturing Science and Engineering. In 2009, SME also published the special issue on Medical Manufacturing [4]. In this paper, biomedical manufacturing was chosen for the topic, because it can be well related to the manufacturing/mechanical engineering programs. This survey paper will introduce its definition and characteristics, and various topics such as biomedical device manufacturing and biomedical product manufacturing. A survey of existing biomedical manufacturing related courses in the manufacturing/mechanical engineering programs will be presented. The contents of these courses often contain an overview of anatomy,

physiology, tissue and biomaterials, US FDA's good manufacturing practice (GMP), and medical devices.

2. Definition and characteristics of biomedical manufacturing

What is 'biomedical manufacturing'? According to Shih [3], biomedical manufacturing is "the applications of manufacturing technology to advance the safety, quality, cost, efficiency, and speed of healthcare service and research." He specified two areas in biomedical manufacturing: biomedical device manufacturing and biomedical product manufacturing. Biomedical devices are defined as products which are used for medical purposes in patients, diagnostics, therapy, or surgery. Such devices include tongue depressors, medical thermometers, and X-ray machines. Biomedical products are defined as products used for the human body, medical operations and healthcare services. Such products include metallic implants and tissues.

Another related aspect to biomedical manufacturing is Biofabrication. As defined by Dr. W. Sun from Drexel University, Biofabrication is to use cells or biologics as the basic building blocks in which biological models, systems, devices and products are manufactured. Biofabrication techniques encompass a broad range of physical, chemical, biological, and/or engineering process, with various applications in tissue science and engineering, disease pathogeneses and drug pharmacokinetic studies, biochips and biosensors, cell printing, patterning and assembly, and emerging organ printing [Biofabrication scope]**.** Biofabrication is an active research field. Many new processes and products are being developed.

Compared with traditional manufacturing, six unique characteristics of biomedical manufacturing were identified: 1) highly regulated products and services, 2) highly connected to the insurance and legal sectors, 3) low ratio of material and manufacturing cost to sale price, 4) no-mistake manufacturing, 5) just-in-case production system, 6) high level of facility management [3]. However, the fundamental technical knowledge and core engineering skills required are the same for both traditional manufacturing and biomedical manufacturing.

3. Examples of existing biomedical manufacturing education curricula

There are a few manufacturing/mechanical engineering programs that offer biomedical manufacturing related topics in their existing curricula. Four examples will be introduced in this paper. The first two examples are the program-level curricular where the series of biomedical manufacturing courses have been designed for the MfgE/ME undergraduate students. The last two examples are the individual courses where individual MfgE/ME faculty developed a course or a lab project in biomedical manufacturing.

Example 1: Biomedical Engineering Specialization Program at University of Calgary [5]

The Engineering Programs at the University of Calgary offers the Biomedical Engineering Specialization program, which allows undergraduate engineering students to take a series of biomedical engineering classes on top of the regular engineering classes. This group of students is called 'the Biomedical Engineering Specialization students.' They are from various engineering disciplines including MfgE/ME and can earn the BSc degree in ME/MfgE with biomedical engineering specialization. The Biomedical Engineering Specialization students in the MfgE/ME programs should take up to 6 biomedical courses in addition to the MfgE/ME courses. Also the Biomedical Engineering Specialization students are required to do an internship and write a thesis or conduct a biomedical research project during their senior year. Table 1 shows the list of Biomedical Engineering courses that are available for the Specialization students.

Table 1 List of courses available for the Biomedical Engineering Specialization students at University of Calgary

	Prefix	Course Title
Biomedical Engineering Core Electives	Biomedical Engineering 405	Biological Tissue and System Mechanics
	Biomedical Engineering 407	Cell Culture and Tissue Engineering
	Biomedical Engineering 409	Bioelectricity
Biomedical Engineering Approved Technical Electives	Biomedical Engineering 509	Introduction to Biomedical Imaging and Applications
	Biomedical Engineering 511	Biomaterials and Biocompatibility
	Biomedical Engineering 513	Photogrammetric Techniques for Reconstruction and Manipulation of Biomedical Data
	Biomedical Engineering 515	Bioengineering Methods in Systems Biology and Physiology
	Biomedical Engineering 517	Biomedical Device Development
	Biomedical Engineering 519	Special Topics in Biomedical Engineering
	Chemical Engineering 535	Principles of Biochemical Engineering
	Electrical Engineering 563	Biomedical Signal Analysis
	Mechanical Engineering 523	Biomechanics of Joints

Example 2: Biomanufacturing Training and Education Center at North Carolina State University [6].

The Center was designed to serve the needs of the biomanufacturing industry and the activities range from biomanufacturing-related courses offered for college and pre-college students to customized training for industry groups. For undergraduate education, the Center offers the University Certificate in Biomanufacturing, which is designed both for NC State students and for persons from outside the University who wish to gain a recognized competence listed on an NC State transcript without relying on a lengthier program such as a minor. The students are required to complete 12 credits in biomanufacturing related courses. Table 2 shows the courses offered by the Center.

Table 2. List of courses available at the Biomanufacturing Training and Education Center at North Carolina State University

	Prefix	Course title
Prerequisite Courses to Enter the Program	BEC (MB) 320	Fundamentals of Microbial Cell Culture
	MB 352	General Microbiology Lab
	BIT 410	Manipulation of Recombinant DNA
Base Biomanufacturing Sequence (2 courses required)	BEC(MB) 420	Fundamentals of Microbial Cell Biotransformations
	BEC 330	Principles and Applications of Bioseparations
	CHE(BEC) 463	Fermentation of Recombinant Microorganisms
Biomanufacturing Specialization (2 courses required)	BBS 426	Industrial Microbiology & Biomanufacturing Laboratory
	BEC 480	cGMP Fermentation Operations
	BEC 436	Introduction to Downstream Process Development
	BEC 485	cGMP Downstream Operations
Elective Courses (4 credits required)	GN 311 - Principles of Genetics, 4 credits; BAE(BBS) 425 - Industrial Microbiology and Bioprocessing, 3 credits; BBS 426 - Industrial Microbiology & Biomanufacturing Laboratory, 2 credits; BCH 451 - Principles of Biochemistry, 4 credits; BEC 436 - Introduction to Downstream Process Development, 2 credits; BEC 442 - Insect Cell Protein Expression, 2 credits; BEC 462 - Bionanotechnology Laboratory, 2 credits; BEC(CHE) 463 - Fermentation of Recombinant Microorganisms, 2 credits; BEC 475 - Global Regulatory Affairs for Medical Products, 3 credits; BEC 480 - cGMP Fermentation Operations, 2 credits; BEC 485 - cGMP Downstream Operations, 2 credits; BEC 488 - Cell Culture Engineering, 2 credits; BEC 497 - Biomanufacturing Research Projects, 1- 2 credits; BIT 410 - Manipulation of Recombinant DNA, 4 credits; BIT 466 - Animal Cell Culture technique, 2 credits; BIT 470 - Advanced Animal Cell Culture: Bioreactor Culture, 2 credits; BME(BEC) 483 - Tissue Engineering Technologies, 2 credits; MB 455 - Microbial Biotechnology, 3 credits	

Example 3. Biomedical manufacturing course at University of Michigan

The ME program at the University of Michigan offers a senior/first-year-graduate level course entitled “Bio-medical Design and Manufacturing” taught by Prof. Shih [3]. This one semester course has three sections and the topics covered in each section are shown in Table 3.

Table 3 Topics covered in Prof. Shih’s Bio-medical Design and Manufacturing course

Sections	Instruction styles	Topics covered
Section 1 (last 6 weeks)	Lectures by the instructor	An overview of anatomy, physiology, tissue-biomedical interactions, regulatory science, FDA GMP, manufacturing processes and systems for medical devices, and financial and operational functions in healthcare services.
Section 2	Seminars given by guest physicians and healthcare personnel	Cardiovascular technology, surgical instruments, orthopedics and implants, endoscopy, neurosurgery, medical imaging, biomedical materials, hospital materials and patient scheduling and flow, etc.
Section 3	Field trips	Students visit health care centers and medical device manufacturers.

Example 4. Biomedical Manufacturing project at a biomedical engineering course in University of North Carolina, Chapel Hill.

Prof. Robert G. Dennis, Associate Professor of Biomedical Engineering offers a junior-level course in Design and Manufacturing [7]. This course has a biomedical manufacturing project lab, which allows students to manufacture a rotating biochamber (See Figure 1). In order to complete their projects, students should use several different manufacturing processes including laser cutting, drilling, welding, rapid prototyping (FDM), surface finishing, heat treatment, sheet-metal working, CNC milling/turning, and mechanical assembly.

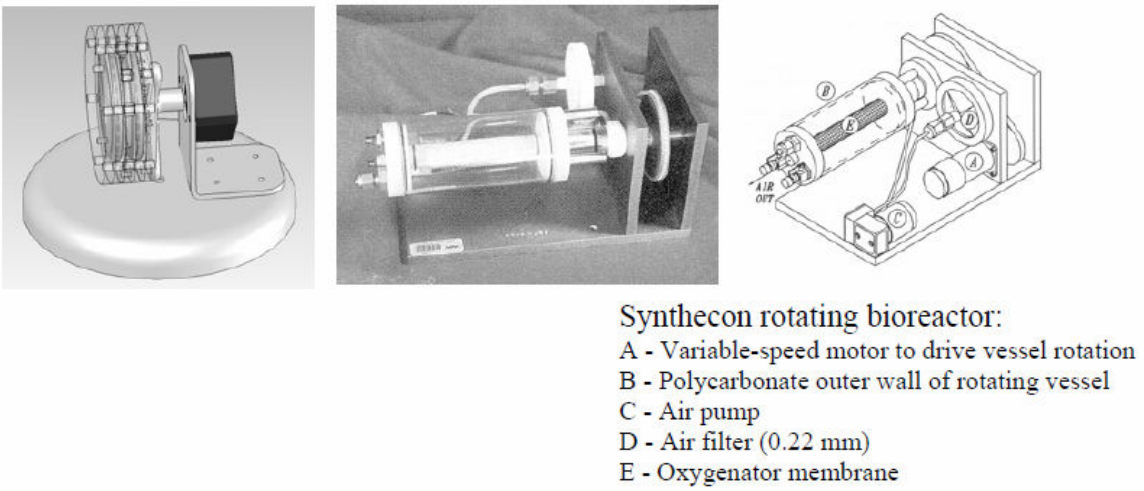

Figure 1. Final assembly drawings and the picture of the rotating biochamber used in Prof. Dennis's course.

4. Common topics for biomedical manufacturing curricular

After surveying biomedical manufacturing related courses and lab activities, there are four common topics covered across the programs. Each topic will be briefly described in this section.

4.1 US FDA's Good Manufacturing Practice (GMP) for medical devices [8]

GMP refers to the Good Manufacturing Practice Regulations promulgated by the US FDA under the authority of the Federal Food, Drug, and Cosmetic Act. The GMP regulations cover a wide range of topics; drugs, some food, blood, and medical devices. GMP is sometimes referred as "cGMP" which means current GMP, reminding manufacturers they should use technologies and systems which are up-to-date in order to comply with the regulation. GMP for medical devices was introduced by FDA's Center for Devices and Radiological Health. It has the detailed requirements and guidelines of quality assurance systems for the complete life cycle of medical devices. GMP specified the basic regulatory requirements that US medical device manufacturers must comply with. These requirements include establishment registration, medical device listing, premarket notification or premarket approval, investigational device exemption for clinical studies, quality system regulation, labeling requirements, and medical device

reporting. GMP and the activities (standard of performance, training, reinforcement, audit) associated with it are one common topic in biomedical manufacturing education.

4.2 Fundamentals of anatomy and physiology

Anatomy is a branch of biology and medicine that studies the structure of living things. Anatomy examines the structure of organisms from the molecular level up to the complete organism. [10] The structure and layout of organ systems is the main focus. Macroscopic anatomy would be the key topic to understand. This topic focuses on the structures of an organism that is visible to the naked eye, which excludes the molecular and cellular levels. Anatomy is an important topic because the form dictates function, but the function also requires a certain form. For this reason, having an understanding of anatomy and physiology is equally important.

Physiology is the science of the functioning of living systems. Physiology focuses on how and why a structure functions [11]. The interconnectedness of functions within an organism makes physiology a large field to study. For biomedical applications physiology should be studied down to the molecular level. To have a basic understanding of an organism's structure and how that structure functions is vital for designing a device or product that works with or within an organism.

4.3 Medical device manufacturing

Medical devices range from simple thermometers to complex surgical tools. Most medical devices require precise miniature features with tight tolerances. In particular, surfaces of medical devices in contact with the human body usually require an extremely smooth surface or specialized textures to promote healthy tissue-biomaterial interactions. Also, medical devices consist of advanced metallic, polymer, ceramic, and foam materials, which are often biocompatible. Innovative manufacturing technology should be implemented into converting these advanced material systems into useful medical device components with consistent quality and lower cost [3].

4.4 Bio-products

Bio-product manufacturing requires fundamental knowledge of materials science and cell biology underlying the design of medical implants, artificial organs, and matrices for tissue engineering. Understanding tissue, organ regeneration, biocompatible materials, molecular and cellular interactions with biocompatible materials is important in bio-product design and manufacturing. Biodegradable and bioreplaceable implants are widely applied in medical operations [9]. Design and manufacturing of implants and prostheses based on control of biomaterials-tissue interactions could be introduced in biomedical manufacturing education.

5. Summary

This survey paper introduced a definition and characteristics of biomedical manufacturing and the related curricula offered in the existing programs. There are a few MfgE/ME programs offering biomedical manufacturing related courses in conjunction with bioengineering programs. The contents of the biomedical manufacturing related courses often contain an overview of anatomy, physiology, US FDA's good manufacturing practice (GMP), surgical device manufacturing, and bio-products.

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