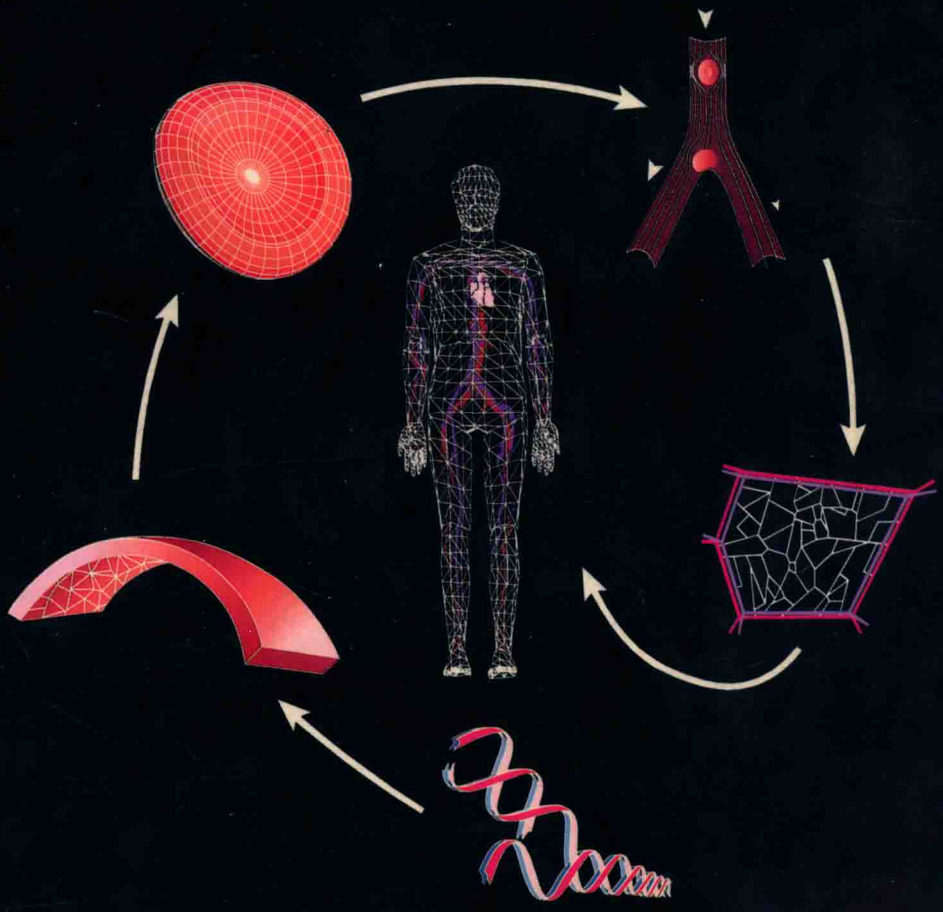
Advanced Series in Biomechanics – Vol. 2

INTRODUCTION TO BIOENGINEERING



Editor

Y. C. Fung

World Scientific

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INTRODUCTION TO BIOENGINEERING

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INTRODUCTION TO BIOENGINEERING

ADVANCED SERIES IN BIOMECHANICS

Editor: Y C Fung *(University of California, San Diego)*

Vol. 1: Selected Works on Biomechanics and Aeroelasticity
Parts A & B
by Y C Fung

PREFACE

This book is written for two purposes: to give beginning students a sampling of the contemporary bioengineering, and to cultivate in the minds of students a sense that engineering is invention and design, is creating things that have never been. Engineering science is the study of nature and humanity quantitatively so that engineering design is made possible. Bioengineering is engineering of living organisms. Bioengineering is very popular, and we have a large number of bright young students. Yet most of them have no idea what engineering is. They think they are majoring in bioengineering, but the University tells them to take more courses in humanities, math, physics, chemistry and biology. Later they will take engineering courses which, at this time, are usually taught very much like traditional math and science: with good lectures, logical presentations, polished derivations, lots of exercises, but no mention of invention. My feeling is that invention and design is the essence of engineering. Invention and design can be taught. A habit of inventive thinking can be cultivated. And the cultivation should begin as early as possible, by demanding the students to invent, and to develop their inventions by design. Hence in this introductory course I ask the students to invent and to design. Invent something, maybe a better mouse trap, a new gadget, a new medical device, a new material, a new drug, a new method, a new instrument, a new experiment, a new theory, a new concept, a new approach. Each new idea needs to be crystallized by a design. I give them assignments to design step by step. They will soon realize that the method must be scientific, and that the real limitation to any important invention is the lack of knowledge. By wanting to invent, they realize that they need to master the classical subjects. Thus the classical subjects become alive, and the study becomes active. Thus I lay great emphasis on the first few pages of this book. The assignments given to the students are the heart of the course. Reading and commenting on the students' papers is the job of the instructor and teaching assistants.

After initiating the student to invent and design, we show them live examples in person of their faculty members. These examples constitute the body of this book. Each example consists of a lecture and a paper. The lecture tells what a faculty member is doing. The paper is the best publication of the speaker. Therefore, this book is not a run of the mill *Introduction* that is supposed to be easy to read and undemanding. Some of the papers selected here are indeed easy to understand. Some others are quite technical and may not be easy to assimilate without proper preparation. All are "advanced" in the sense that they represent a part of the current frontiers of knowledge.

Not everybody likes the inventive approach or the subject of bioengineering. This course may persuade some of the students to choose a different career goal. Our experience in this introductory course has been very satisfying. The final reports handed in by the students are often remarkably well done. Nice, fresh ideas abound. You can see that the inventive chord in the student has been plucked.

The authors and I feel the urge to publish this book because we believe that engineering education needs a qualitative lift. We need to challenge young engineering students to think their own thoughts. We need to bring inventive thinking to the fore. We need to give engineering courses a new spirit, to teach invention, to cultivate independent thoughts, to use science as our tools and to enjoy science the same way as we enjoy humanities. We give

an example here in the subject of bioengineering. Any department in any university can easily remodel our example presented here to suit its own image and ambition.

Recently, several books have appeared bearing the title *Introduction to Bioengineering.* Most of them are big tomes. I cannot see how an instructor can use them to teach a course for the beginners. This book, however, is aimed at the beginner. It has been tried out several times at UCSD, and have been found exciting. We invite other institutions to try it for their students.

Y. C. Fung
Editor

TO THE INSTRUCTOR

This book is not an ordinary textbook. It is a cultural reader trying to tell a beginner what bioengineering is. The authors tell the story through their personal experiences. They do not claim complete balance of their views; but they are sincere, vigorous, and so committed that they are devoting their whole lives to pursue their visions. They know that the field of bioengineering is young, and is developing in many directions. They all believe that the best way to teach introductory bioengineering is to ask the beginners to think about invention and design right away, whatever they think bioengineering is. This is where this little book comes in. Each author asks certain questions, then invents and designs some method to answer their questions. Their lecture notes and papers could serve as models. We recommend a series of assignments to the students as listed in the following pages, and asking them to read the book one chapter per week. We trust that you will find this approach very enjoyable, because your students will be proud of their new found abilities.

TO THE STUDENTS

Hi,

This course is an introduction to the central topics of Bioengineering. The principles of problem definition, team design, engineering inventiveness, information access and communication, ethics and social responsibility are emphasized.

The authors of this book are faculty members of Bioengineering. Each of them presents a short lecture on some of the things they are doing, and a sample of their writing. This volume is a collection of these lecture notes and papers. By meeting your faculty members, listening to them and reading the lecture notes and papers, you will get an idea about their personal interests and achievements. Overall, you will get a feeling about Bioengineering as a discipline.

An objective of this course is to let you learn a little bit about what a bioengineer is expected to do and to behave in the industry. In the industry, you are expected to design and to work in teams with other people. Our course assignments are aimed in this direction.

Bioengineering is a young discipline. It is still developing rapidly. New knowledge is added every day. In the development of new knowledge, the application of the methods and results of classical disciplines is most important. That is why your university asks you to take courses in mathematics, physics, chemistry, humanities, etc. To help you realize that this is the case, I am introducing design as a major approach to bioengineering in this course. You are asked to think yourself. Then you are asked to think with some friends as a team, advancing your project together. At the end of the course, you gain not only some knowledge, but also some friends. That friendship may be the most valuable part of you college eduction.

My philosophy of using design as a major approach to learning science was developed over the years. In the past, students listen to lectures, read textbooks, do exercises, take exams and pass courses with only a vague idea that what is learned is useful. You have done enough of that. Now, in thinking about a design project, you may find that your success depends on certain knowledge about science and humanity. Therefore, you search for knowledge actively.

The reading material accompanying each lecture is a sample of good papers. Each paper talks about a topic of engineering science. These papers are not design reports, but usually they are the results of many successful designs.

On the following three pages are the assignments I gave the class when I was teaching. Your instructor may give you a different set.

Y. C. Fung
Editor

SAMPLE ASSIGNMENTS

Reading: Read a chapter before the class, and the author's paper after the class.

Lecture Schedule: To be presented.

Assignment No. 1 Report Due on:_____

Describe a research project you would like to do. This can be an invention of an instrument for scientific inquiries, or a device for clinical application, or a gadget for home care, or any other things that you think should qualify as Bioengineering. Or it can be a study of a scientific or technological problem concerning a phenomenon of interest to bioengineering. Note that I did not define "bioengineering." You define it yourself. I know most of us have at least a dozen projects we would like to do at any time. For the present assignment, make a choice of one which is your highest priority, one of which you would be most proud if the project were completed successfully. This assignment is to be answered intuitively, based on your "gut feeling." Explain your project as best you can. Describe what it is, why do you think it is important, and how would you approach it, all in **one page**. If the idea is your own, no reference is needed. If the whole idea or parts of it came from another person, or from a journal article, a paper, a book, then you should acknowledge the source with references. Don't ever be caught for plagiarism.

Assignment No. 2 Due date:_____

Embodiment of Your Thoughts on a Design.

Give your design a title. Supply some details with hand drawn sketches or graphics, and explain your objectives, design principles and expectations of its significance. Not to exceed 3 pages.

Important Note:
You are responsible to hand in a typed or neatly handwritten report at the due date specified. Please hand in at or immediately after class. Each page should have a page number and your full name clearly printed at the upper right corner. Use 8.5×11 inch sheets of plain paper. Sign and date the paper at the end. Neatness and timeliness are essential quality of a good engineer.

Assignment No. 3 Due date:_____

Report on Team Organization and Team Project.

Teamwork is encourged. Get several friends to work together. Discuss your projects to see if you can reach a consensus to concentrate on **one** project. If you can, then revise Reports to Assignments 1 and 2 into a team report, and write Reports to Assignments 4–8 together as a team. On the upper right hand corner, write down the names of all team members. If you decided to go at it alone, it is OK. In that case, turn in an improved version of Reports 1 and 2, with greater details.

Assignment No. 4 Due date:_____

Library Search.

Present references that you have found.
Not to exceed 2 pages.

Assignment No. 5 Due date:_____

Design.

Discuss the scientific basis of your design in light of library search. Discuss the feasibility and difficulties. Estimate time needed to accomplish your design. Discuss possible ethical questions involved.
Report, maximum 2 pages.

Assignment No. 6 Due date:_____

Illustrate your design with good graphs. Explain your drawings carefully. If your work is theoretical, develop your equations with sufficient details.

Assignment No. 7 Due date:_____

Discuss the feasibility of your design or research. What are the unknown factors? What may cause your design to fail? What are its strengths? What are its weaknesses? How are you going to test your design? Do you need animal experiments? Do you need human experiments? What are the governmental and university regulations with regard to these experiments?

Assignment No. 8 Due date:_____

Final Report.

Prepare a final report based on all you have written up to this point. Use the following format for the cover page:

(a) At top:
Final report on Course BE1, Introduction to Bioengineering Instructor's name:
(b) At center: Title of your project
(c) The names of all the authors in alphabetical order
(d) At bottom: Date submitted

Beginning on page 2, write Sections in the following order:

Introduction
Specific Aims
Designs and Analysis
Discussion
References

This final report will be retained by the department. It will not be returned to you. Please save a xerox copy for yourself.

Write the best you can. Make it a nice little paper for future reference.

Reports Expected

You are responsible to hand in a clearly written report on each item listed below at the due dates specified. Each page should have a page number and your full name clearly printed at the upper right corner. Sign and date the paper at the end.

Report 1	Proposal of a Design Project	1 page
Report 2	Embodiment of my Thoughts in a Design on...	Not to exceed 3 pages
Report 3	Scientific Basis of My/Our Design On... Team work is encourged. Get several friends to work together. Discuss your projects to see if you can reach a consensus to concentrate on **one** project. If you can, then revise Reports 1 and 2 into a team report, and write Reports 4–6 together as a team. On the upper right hand corner, write down the names of all team members.	Max. 3 pages
Report 4	Results of Library Search on My/Our Project on...	Not to exceed 2 pages
Report 5	Estimate of Time and Money Needed to Accomplish My/Our Design on... and Possible Ethical Question Involved	Max. 2 pages
Report 6	Team and Individual Final Report on the Design of... Collate your five reports together. Correct all errors and misprints. Improve the English.	A nice paper

CONTENTS

Appendixes

CHAPTER 1

ROLES OF FLOW MECHANICS IN VASCULAR CELL BIOLOGY IN HEALTH AND DISEASE

SHU CHIEN

Departments of Bioengineering and Medicine, and
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University of California, San Diego

Endothelial cells (ECs) form the inner lining of blood vessels, separating the circulating blood from the remainder of the vessel wall. Endothelial cells not only serve as a permeability barrier to regulate the passage of molecules between blood and the vessel wall, but also perform many important functions, including the production, secretion, and metabolism of many biochemical substances and the modulation of contractility of the underlying smooth muscle cells. The responses of endothelial cells and smooth muscle cells to changes in pressure and flow play a significant role in regulating the functional performance of blood vessels in health and disease.

Atherosclerosis results from the accumulation of fatty materials as atheroma in the artery wall. Atherosclerotic narrowing of the vessel lumen can cause a reduction of blood flow in the organ supplied by the vessel, thus leading to clinical problems. Examples are stroke, heart attack, and walking difficulty, which result from severe reductions of blood flow to the brain, heart, and legs, respectively.

There are two major elements in the initiation of atherosclerosis (Fig. 1). The first is lipids, especially the low density lipoprotein (LDL), which can become oxidized in the vessel wall. The second is monocytes, which become transformed into macrophages (large

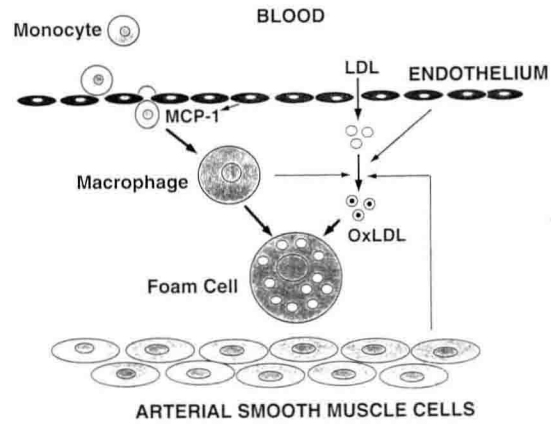

Fig. 1. Schematic drawing showing the roles of low density lipoprotein (LDL) and monocytes in the formation of foam cells.

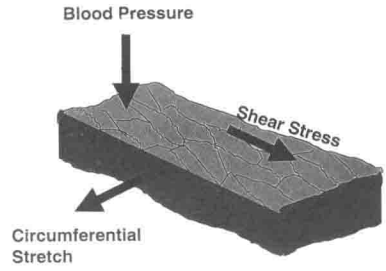

Fig. 2. The hemodynamic forces acting on the blood vessels due to blood pressure and flow.

eating cells) after entering the artery wall. The macrophages can engulf oxidized LDL to form foam cells, and the accumulation of foam cells in the vessel wall is the basis for the formation of atheroma (Steinberg, 1995).

Although every part of the arterial tree is exposed to the same LDL concentration in the circulating blood, atherosclerotic lesions show preferential distributions in branch points and curved regions (Cornhill *et al.*, 1990), suggesting that local variations in hemodynamic forces play a significant role in the focal nature of the lesions (Nerem *et al.*, 1993). Work done in our and other laboratories indicate that hemodynamic factors modulate both the transendothelial passage of large molecules such as LDL and the entry of monocytes into the artery wall. There are several components of hemodynamic forces (Fig. 2). This chapter focuses on the effects of shear stress, which is the tangential forces acting on the luminal surface of the vessel as a result of flow. Other important forces are the normal stress and circumferential stress resulting from the action of pressure. The aims of studying the role of hemodynamic forces in the regulation of EC function are to elucidate (a) the fundamental mechanism of mechano-chemical transduction, and (b) the biomechanical and molecular bases of the preferential localization of atherosclerosis in the arterial tree.

1. Role of Hemodynamic Factors in Transendothelial Permeability of Macromolecules

At the branch points and curved regions of the arterial tree, which have a predilection for atherosclerosis, blood flow is unsteady and the shear stress shows marked spatial and temporal variations (Glagov *et al.*, 1988). Weinbaum *et al.*, (1985) proposed the hypothesis that complex flow patterns cause an accelerated EC turnover (including cell mitosis and death), such that the resulting leakiness around the ECs undergoing turnover increases the permeability of large molecules (e.g. LDL) across the endothelial layer. Our experimental studies have provided evidence that EC mitosis (Chien *et al.*, 1988; Lin *et al.*, 1989) and death (Lin *et al.*, 1990) are associated with the leakage of macromolecules such as albumin and LDL on individual cell basis. Studies performed in a number of laboratories, including our own (Schwenke and Carew, 1988; Chuang *et al.*, 1990; Truskey *et al.*, 1992) have shown that these events of accelerated EC turnover occur primarily in areas with disturbed blood flow, e.g. arterial branch points. Electron microscopic studies (Fig. 3) have identified the widening of the intercellular junctions around ECs which are dying or undergoing mitosis (Huang *et al.*, 1992; Chen *et al.*, 1996).