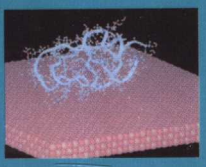

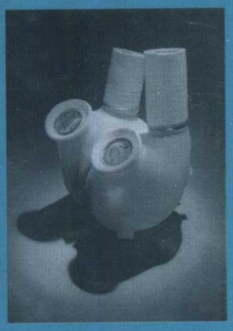

Biomedical Devices and Their Application

生物医学工程及应用

时东陆　主编

清华大学出版社

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北京

内 容 简 介

本书是“生物材料和生物技术”丛书中的第 2 本。本丛书提供了在生物材料和生物技术领域最新的信息。它的重点是阐述在这些领域的基本原理和最近的发展。本册书共有 5 章，分别是：药品运送中的生物材料、对现有的药品运输类型及其在治疗局部病变的临床作用、蛋白质电泳技术及其应用、模拟雌激素的化学药品以及生物技术在医学工程中的应用。这本书可作为材料、生物、医学等相关专业大学高年级学生及研究生的参考教材，也可供科研人员阅读。

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21世纪科技前沿丛书
Frontiers of Science and Technology for the 21st Century

《Frontiers of Science and Technology for the 21st Century》

FOREWORD

Over the next several years, Tsinghua University Press will publish a series of books addressing progress in basic sciences and innovations in technology. We have made no attempt to pursue a comprehensive coverage of all disciplines of science and technology. Rather, topics for this series were selected with an emphasis on the currently active forefront of science and technology that will be contemporary in the next century. Most books in this series will deal with subjects of cross disciplines and newly emerging fields. Each book will be completed by individual authors or in a collaborative effort managed by an editor(s), and will be self-consistent, with contents systematically focused on review of the most recent advances and description of current progresses in the field. Sufficient introduction and references will be provided for readers with varying backgrounds. We have realize clearly the challenge of encompassing the diverse subjects of science and technology in one series. However, we hope that, through intensive collaboration between the authors and editors, high standards in editorial quality and scientific merit will be maintained for the entire series.

The international collaboration on this series has been coordinated by the Association of Chinese Scientists and Engineers-USA(ACSE). In the science community, authors voluntarily publish their results and discoveries in the full conviction that science should serve human society. The editors and authors of this series share this academic tradition, and many of them are fulfilling a spiritual commitment as well. For our editors and authors who were graduated from universities in China and further educated

abroad in science and engineering, this is an opportunity to dedicate their work to the international education community and to commemorate the historical open-door movement that began in China two decades ago. When the human society enters the information age, there is no geographic boundary for science. The Editorial committee hopes that this series will promote further international collaboration in scientific research and education at the dawn of the new century.

The Editorial Committee
1999.6

《21 世纪科技前沿》

丛书序言

由清华大学出版社出版的这套丛书是基础科学和应用科学领域内的专门著作。除了可作为研究生教材外，也可作为科研和工程技术人员的参考书。在丛书的题材选择中，着重考虑目前比较活跃而且具有发展前景的新兴学科。因此，这套丛书大都涉及交叉和新兴学科的内容。编写的方式大多由主编策划并组织本学科有影响的专家共同执笔完成，从而使每一本书的系统性和各章节内容的连贯性得到了充分的兼顾。丛书涵盖学科的最新学术进展，兼顾到基本理论和新技术、新方法的介绍，并引入必要的导论和充分的参考文献以适应具有不同学术背景的读者。编撰一套容纳多学科的科技丛书是一项浩繁的工作，我们希望通过主编和作者的集体努力和精诚协作，使整套丛书的学术水准能够保持在较高的水平上。

编辑《21 世纪科技前沿》丛书是由“旅美中国科学家工程师协会”发起的一项国际科技界的合作。传递信息，加强交流，促进新世纪的科技繁荣是编著者们参与此项工作的共同信念。此外，这套丛书还具有特别的纪念意义。20 年前，历史的进程使成千上万的中国学生、学者有机会走出国门，到世界各地学习和从事科学研究。今天，活跃在世界科技前沿领域的中华学子们没有忘记振兴祖国科技教育事业的责任和推动国际学术交流与合作的义务。正是基于这一共同的心愿，大家积极参与这套系列丛书的撰写、组稿和编辑工作。为此，我们愿以这套丛书来纪念中国改革开放 20 周年。

编 委 会

1999. 6

Preface

Biomedical devices that contact with blood or tissue represent a wide range of products. Depending on their potential harm to a body, medical devices are categorized according to the degree, so their safety can be assured. All biomaterials are by definition designed to contact with a body for a certain period of time. The nature of the body contact, as well as the duration a material contacts with the body may initiate unwanted biological responses. In comparison with invasive devices (like catheters and medical implants contact directly with tissue or with the circulating blood) non-invasive devices (like wound-dressings and contact lenses contact with the skin, the sclera, and the mucosa or with open wounds) have a lesser risk of hurting a patient.

When blood contacts with a foreign material, plasma proteins become absorpted to the surface within a few seconds. The reactions that follow, the so-called intrinsic pathway lead to the formation of fibrin and activation of platelets and white blood cells, result in blood clot formation. The longer the contact time, the higher the chance the coagulation system becomes activated. Therefore, for a long time engineers of blood pumps focussed only on optimizing the shape of the inside of the pump in their efforts to prevent low-flow conditions and stagnating flow zones. With the introduction of the electromechanical driven pump systems and the clinical demand of chronically implantable heart assist devices, the external shape of the device and the kind of materials used in the pump housing became as important. After pump insertion, the (continuously moving) lungs surround the pump and can easily become traumatized. Traumatized lungs may collapse (atelectasis), get infected (pneumonia) or can leak air (pneumothorax). Also, the material of the pump housing must prevent that the lungs get adhered to the material.

In the artificial larynx, shape and used materials are as important. In this kind of biomaterials application, shape is defined not only by the anatomical dimensions the device should fit in but also by the surgical insertion technique that must be applied to position the device, as well as by the physical and psychological acceptation of a device by a patient. A tissue connector placed between the trachea and esophagus, for fixation of the tracheal-esophageal shunt valve, needs a certain size and shape to ease

surgical positioning. The tracheo-esophagal shunt valve itself, needs a certain size and shape to allow the positioning of a voice producing element in its inside. When the tissue connector is too small, the voice-prosthesis will not fit. When the connector it is too large, the esophagus becomes partially compressed, resulting in feelings of discomfort or swallowing disorders. Whereas in the use of implantable blood pumps tissue ingrowth must be prevented, in tissue connectors a tight tissue ingrowth is just wanted. Based on its intentional use, surfaces of the different devices require different surface characteristics. Finally size and shape of a visible device like the tracheo-stoma valve, a device that allows a patient hands-free closing of the tracheostoma, are important in a different way. A large valve positioned on top of the tracheostoma opening may function better than a small valve. However, the large valve will attract more attention fromthird person and therefore makes patients that have to wear these devices feel uncomfortable. The shape and selected materials also depend on preferred manufacturing techniques and the physical properties of the material. Many materials that possess the optimal physical properties, often cannot be used because for a specific application because of their improper biocompatibility characteristics. Materials, size and shape all play a crucial role in the biomaterials applications described in this chapter. The given overview is not complete. During the processing of the book various new applications will have been developed and tested. The latest developments can be traced in the various scientific journals that have been enlisted in the references or in various medical textbooks.

We intend this book to provide up-to-date information in the field of biomedical devices and their applications. The focus of the book is the basic concepts and recent developments in this field. The book will cover a broad spectrum of the topics that include drug delivery, protein electrophoresis techniques, medical devices, and the environment that mimics estrogens. Most of the critical issues are addressed in a straightforward manner so that nonspecialists and university students can benefit from the information. Furthermore, many novel concepts in biomaterials are explained in the light of current theories. An important aspect of the book lies in its wide coverage of biomedical applications.

The book is written for a large readership including university students and researchers from diverse backgrounds such as orthopedics, biochemistry, bioengineering, materials science, tissue engineering, and other related medical fields. Both undergraduate and graduate students will find the book a valuable reference not only on biomedical devices, but also

on some important biotechnology topics. Thus, it can serve as a comprehensive introduction for researchers in biomedical science and engineering in general, and can also be used as a graduate-level text in related areas.

Chapter 1 presents the most recent experimental results on medical devices. In this chapter techniques that can be used to decrease the time of development of medical devices are discussed: multidisciplinary approaches in conducting research, medical technology assessment, constructive medical technology assessment and concurrent engineering techniques. Also the use of computer-supported group-decision techniques based on the analytic hierarchy process is illustrated. Finally three research areas are highlighted: mechanical circulatory assist devices, devices that contribute to voice rehabilitation for laryngectomised patients and extendable orthopaedic endoprostheses. The advances that have been made during the past decades will be discussed.

Chapters 2 and 3 are devoted bo biomaterials in drug delivery. They give details of materials preparation, experimental procedures, and novel methods for special ways of drug delivery. A major research thrust in the pharmaceutical and chemical industry is the development of controlled release systems for drugs and bioactive agents. Many of these delivery systems in use and under development consist of drugs dispersed within a polymeric carriers. These carriers are designed to release the drugs in a controlled fashion for times ranging from minuted to years. The emphasis on the development of novel controlled-release devices is in response to the discovery and production of new drugs in today's expanding biotechnology fields. However, due to the cost of production, it is imperative to develop new methods to deliver these drugs in the most effective manner. A major limitation in the pharmaceutical industry is that the current methods for drug delivery, such as injections, tablets and sprays, may not be the most effective method of delivery for certain drugs and as a result, multiple administrations may be required to keep the concentration of the drug in the blood at a therapeutically effective level for reasonable periods of time. Typically with these types of administration, the drug levels rise to a maximum and fall off to a minimum value, at which time another dosing of the drug is required. This is problematic for drugs with a narrow range of therapeutic concentration as the drug levels will continually rise above the effective range into the toxic region during which time increased adverse side effects are likely, and then fall below the minimum effective concentration, during which time the drug is not effective. The goal of

Chapter 3 is to give a general review of the types of drug delivery systems available and discuss the clinical application of these systems to treat localized disease states.

Chapter 4 should be of great interest to researchers studying protein electrophoresis techniques. This chapter reviews the fundamental concepts in protein electrophoresis from the standpoint of the biomaterials scientist. It describes an array of experimental techniques that, while quite familiar to the molecular cell biologists, are usually novel to the biomaterials scientists. It also deals with the author's applications of some of the techniques of protein electrophoresis. The purpose of this chapter is to illustrate by example how one biomaterials researcher sorted through the electrophoresis "palette" and made experimental design decisions.

Chapter 5 deals with chemicals in the environment which mimic estrogens. Estrogens are steroid hormones that are produced by the female gonads and have widespread effects throughout the body. Males also produce small amounts of estrogens by conversion (aromatization) of the male sex hormone testosterone and are sensitive to estrogenic effects. The primary organs that are targeted by estrogens are components of the neuroendocrine-reproductive axis and include the hypothalamus (ventral part of the midbrain), pituitary gland (the master endocrine gland), and the reproductive tract, e.g. uterus and vagina in females and prostate in the male. Other tissues, including mammary glands, cardiovascular system, bone and skin, are also responsive to estrogens, underscoring the profound capability of these compounds to influence most bodily functions.

All authors are prominent researchers and have extensive research experience in diverse fields of biomedical science and engineering. We are grateful to them for these important contributions from which, we trust, many readers shall benefit significantly.

Donglu Shi
Cincinnati
March, 2003

前　言

我们编写此书的目的是给读者提供生物医学工程及应用领域最新的信息。重点是介绍生物医学工程及应用的基本概念和目前的进展。此书介绍了药品运送，蛋白质电泳，医疗器械和雌激素模拟技术。书中根据当前的理论解释了很多生物医学工程及应用领域的概念。重要的是，介绍了很多生物医学工程的实际应用。不仅介绍了现代医学尖端的技术，而且介绍了一些生物医学工程及其在医学领域独特的应用。

此书内容介绍大多浅显易懂，适合于不同专业背景的读者群，包括相关医学领域的大学学生和研究人员。它不仅可作为本科生和研究生学习生物医学工程及应用的参考书，而且也可充当研究组织工程学相关课题的参考书。

全书分为 5 章。第 1 章和第 2 章主要是关于生物材料在药品运送中应用。书中详细介绍了药品运送中材料的准备，步骤和新颖的方法。在药物和生物制药工业中，主要的研究方向是药品和生化药品经销商有控制的发放系统。现在正在使用的和正在开发的药品运输系统都是将药品分散在聚酯容器内，这些容器可以控制药品的发放时间从分钟到年。开发一种新的控制发放方式，重点是针对在今天的生物科技发展领域，新的药品的发现和制造的需要。第 1 章讲述了水凝胶的结构和特性，它可应用在有控制的药品运输领域。第 2 章介绍了现有的药品运输类型，并讨论了这些系统在治疗局部病变的临床作用。

第 3 章研究蛋白质电泳的人应该很感兴趣。此章讲述了生物材料科学家对蛋白质电泳现象的解释。也介绍了一系列的实验技术，虽然对分子细胞生物学家来说并不陌生，但是对生物材料科学家来说却比较新颖。另外也介绍了电泳应用的技术。此章图例说明了一个生物材料研究员怎样通过电泳调色板分类，并得出实验结果。

第 4 章讲述可以模拟雌激素的化学药品。雌激素是女性身体性腺产生的类固醇荷尔蒙，并对身体产生广泛的影响。男性体内雄性荷尔蒙也可转化为少量的雌激素，并对性交配敏感。首先对雌激素反应的器官是神经生殖中轴和视丘下部(中脑的腹侧)。垂体腺(内分泌腺)和生殖器，乳腺，心血管系统，骨头和皮肤，也会对雌激素起反应。

第 5 章介绍了最近医疗器械的实验结果。首先，介绍了以下几种可以缩短医疗器械开发时间的技术：进行研究的多学科研究方法，医疗技术评定，建

设性的医疗技术评定和目前的工程技术。其次也以图例说明了基于分层分析的计算机支持技术。最后重点介绍了三个研究领域：帮助咽喉病人声音复原的医疗循环辅助设备和整形外科。也介绍他们在过去几年中治疗的积极作用。

我们希望这本书能给大家提供生物医学工程及应用一些实时的有用的信息。

借此对所有参与此书编著的作者表示衷心感谢。

时东陆
2003.6

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