

微纳技术著作丛书（影印版）

# 生物微机电系统

BioMEMS

Gerald A. Urban



科学出版社

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## 内 容 简 介

微系统技术领域的飞速发展在许多重点学科（从微电子到生命科学）引入了极具前景的产品，特别是生命科学和卫生保健业，一直是人们期望的微系统技术产品的主要市场。毫无疑问，生物学和微纳科学的结合将会制造一场新的科技革命。器件的微型化，直到纳米级别，接近生物组织的大小，将是生命科学成功的必备条件。从长远角度来看，生物技术和微纳技术的结合将使人们对细胞和整个生物体的功能有更深的见解。本书对生物微系统进行了简单的回顾，并把微纳米技术广泛渗透到生物和医学领域，这对未来科学和生命科学新产品的发展进程是十分必要的。

本书适于生命科学、系统生物学、生物工程学和微纳米系统工程等相关领域的大专院校教师、高年级学生、研究生及科技人员阅读参考。

Gerald A. Urban: BioMEMS

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## 序

科学出版社准备出版一套《微纳技术著作丛书》，包括原创作品和引进作品（影印或翻译）两种形式，并聘请专家组成编委会。这是一件大事，希望能坚持把办好。

微纳米技术作为 21 世纪重要的一项技术，已成为国际科学界和工程技术界研究的热点。近年来，微米纳米技术进展迅速，已经发展成为一个包含机械、材料、电子、光学、化学、生物、基因工程、医学等基础学科的综合领域，而不仅仅属于任何单一的科学与技术门类。就其产品而言，也早已超越了人们广为熟悉的微型加速度传感器和纳米碳管等，呈现出向各个科学和技术领域全面渗透的趋势。

由于微纳米技术使得人们除了可以在同一基片上实现包括机械、流体、化学、生物、光学等器件外，也可以将信号处理和传输系统集成在同一基片上用以处理信息，决定计划，控制周围环境，从而大大提高最终产品的综合性能，实现高度智能化。在未来的航空航天、生物医学、环境监控、无线通信、汽车和交通、石油化工、能源、工农业、国家安全、食品和消费的各个领域都将有广泛应用，对国民经济、科学技术、社会发展与国家安全具有重要意义。今后的几十年里，随着微米纳米技术的迅速发展和向现代科学和技术的各个门类渗透，其对我们现代生活的各个方面带来的影响将是长期和深远的。从某种意义上来说，微米纳米技术的发展，可能改变人类的工作和生活方式，乃至基本概念，其潜在的影响有可能和以计算机技术为代表的微电子工业对世界的影响相提并论。

正是由于其诱人的应用前景和巨大的潜在市场，微米纳米技术目前已成为世界各国大力投资进行研究和发展的热点领域，其研究范围包括了材料、器件和系统，涉及的技术包含机理研究、设计分析、计算仿真、制造工艺、系统集成或组装、测控技术和应用研究等。随着微纳米技术的迅猛发展，近年来国外有大量这方面的专业书籍出版。

《微纳技术著作丛书》涵盖材料开发、系统设计、检测技术、集成技术、通信网络、传感系统、微加工技术等方面，它们都是本领域的研究热点。这套丛书的出版对促进我国微米纳米技术的发展将有很大的推动作用。

这套丛书中，原创作品收录的都是国内从事微纳技术的一线研究人员在本领域的研究成果与心得，具有很强的独立性、创造性和系统性。引进作品都是与国际知名的出版集团合作，经国内专家的甄别，挑选出能反映国外最新研究成果、对国内读者又有借鉴价值的作品，具有权威性、前瞻性和可读性。因为微纳米技

术是一个交叉学科领域，我们有意识的选择了一些由多人合写的专著。通常这类著作都是由相关领域的知名专家，各自在每一章节涵盖一个专题，既有进行综合性的论述，也有个人的具体独创性研究。这样的书籍，通常能帮助读者既获得某一领域的研究概况，又能从一个具体的应用专题中获得收益。

2007年初推出的第一批影印版图书，我和王万军教授进行了评读，此套丛书很实用，不少作者在该领域有很高的声望。我们建议致力于微米纳米技术的研究人员，包括研究生、技术人员，能够花些时间阅读。

总之，我们对科学出版社组织出版这套丛书的举措很赞赏，也希望他们能将这一工作认真、长期地做下去。同时，我们也希望国内的专家能够积极、踊跃地加盟，为我国微米纳米技术的推进做出贡献。

周兆英 王万军

2006年12月7日

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## **Preface**

Explosive growth in the field of micro system technology (MST) has introduced a variety of promising products in major disciplines, from microelectronics, automotive, telecommunications, process technology, to life sciences. Especially life science and the health care business was, and is, expected to be a major market for MST products. Undoubtedly the merging of biological with micro- and nano science will create a scientific and technological revolution in the future.

Unfortunately such obvious facts were corrupted in the past by fancy visions, such as micro-submarines swimming in the arterial system repairing calcification of blood vessels. Major financial resources were dedicated to this new and exciting technology. However, the breakthrough, predicted in a 'science fiction'-like prophecy, was significantly delayed as a result of the complexity and difficulties which MST developments faced in life science applications. This led to some misunderstandings of the real benefits of this technology and of the outcome for clinical science.

MST on its own is now becoming established, and it will be valuable to look at the lessons of the past, the practical issues, and the future expectations for life science applications.

Therefore the aim of this review is to gain a realistic view of this topic. In this book we shall display most of the important bio-related MST activities, and it will become obvious that micro miniaturization of devices, down to the nano-scale, approaching the size of biological structures, will be a prerequisite for the future success of life sciences. Microminiaturized analytical and therapeutic micro- and nano-systems will be mandatory for system biologists in the long run, in order to obtain insight into morphology and the interactive processes of the living system. This is the topic of system

biology, a new and very challenging research field investigating the whole complex functionality of a living system. With such a deeper understanding new and personalized drugs could be developed leading to a revolution in life science. However, the present tools for these scientific tasks are macro devices, such as MS or NMR equipment. The development of smart and sensitive micro analytical tools, ultimately with single molecule sensitivity, is obviously future MST tasks.

Up to now, micro analytical devices are used in clinical analytics or in molecular biology as gene chips. In addition, standard micro biomedical products are employed in intensive care and the surgical theatre mainly for monitoring purposes. However, the gap between these two completely different scientific fields will be closed as soon as functional micro-devices can be produced allowing a deeper view into the function of cells, cell cultures, organs, and whole organisms.

Despite that the word 'micro system' has become an established and commonly used term, it is still lacking a generally accepted definition. Some definitions emphasize more the micro miniaturization, others prefer a technology based view, while the third kind highlight the system aspect. Although the latter aspect is obviously a profound one, the others need still to be considered. Undoubtedly, miniaturization is a key feature of MST, yielding a significant benefit for applications in the biosciences and in space projects. In all other applications system specifications and costs, rather than miniaturization, have first priority.

A new discipline evolved which focused on micro systems for living systems. Historically micro systems for automotive or computer periphery applications were called **MicroElectroMechanical Systems (MEMS)**, since such micro-parts exhibited mechanical structures in acceleration and pressure sensor systems or micro-elements for actuating fluids. The combining of MEMS with biology and medicine created the common term 'BIOMEMS', although only in a few applications are mechanical movable structures used.

Another important aspect of BIOMEMS devices is—despite the miniaturization—the use of innovative materials and biological substances in combination with micro-technological fabrication processes. The combination of these topics yielded completely new sensor devices, the so called 'micro biosensors'. Examples of early realized miniaturized analytical BIOMEMS are glucose sensors, now well established in diabetology for home care measurement of diabetics, generating a fast growing market of several billion dollars.

In the latter years another market pull for micro-biosensor devices was generated in the United States for measuring warfare agents, food and environmental safety. The 'Homeland Security Program' is providing

substantial funds for the development of micro- and nano technology based handheld monitors for ubiquitous use.

These BIOMEMS product successes point to the enormous potential of miniaturized devices which have historically always been of leading research interest. The initial stages of BIOMEMS developments can be found in the micro-sensor developments of the mid 20<sup>th</sup> century, whilst complete BIOMEMS based products just recently started to penetrate significant medical markets, illustrating the complexity and the difficulties of transferring a new technology into new products for large medical markets.

The first chapter offers an overview of the basics and the historical background of BIOMEMS. Owing to the interdisciplinary character of BIOMEMS, different topics are presented in what follows in order to provide an overview of the broad BIOMEMS development field. The scientific topics range from implant devices to analytical micro-biosensors systems, complex DNA based micro systems, analytical protein arrays, and cell based systems. Some of the necessary technological prerequisites are micro-fluidic platforms and separation based tools on chips.

As a view into the future of the emerging fields of whole tissue based arrays, as well as bio-nano-technology, research results are highlighted. These most interesting scientific research fields are expected to yield exciting research results and long awaited products for the next decade, particularly in the direct intra-cellular observation of metabolic pathways using nano-tools. The understanding of these complex functions will be a prerequisite for the developments in two emerging fields, system biology and BIONEMS—**BI**ological **N**ano-**E**lectro**M**echanical Systems.

Subsequent book editions will undoubtedly deal with such topics in more detail.

In this book the reader will be able to review at a glance the exciting field of bio microsystems, from their beginnings to indicators of future successes. This book will also show that a broad penetration of micro- and nano-technologies into biology and medicine will be mandatory for future progress of scientific and new product development in life science.

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