BioMEMS and Biomedical Nanotechnology

Volume IV
Biomolecular Sensing, Processing and Analysis

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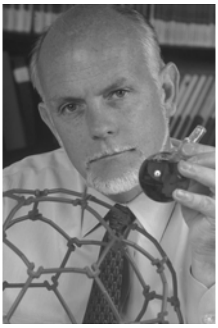
Dedicated to Richard Smalley (1943–2005), in Memoriam



To Rick,

father founder of nanotechnology
prime inspiration for its applications to medicine
gracious mentor to its researchers
our light—forever in the trenches with us

(Rick Smalley received the 1996 Chemistry Nobel Prize
for the co-discovery of carbon-60 buckeyballs)

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Foreword

Less than twenty years ago photolithography and medicine were total strangers to one another. They had not yet met, and not even looking each other up in the classifieds. And then, nucleic acid chips, microfluidics and microarrays entered the scene, and rapidly these strangers became indispensable partners in biomedicine.

As recently as ten years ago the notion of applying nanotechnology to the fight against disease was dominantly the province of the fiction writers. Thoughts of nanoparticle-vehicled delivery of therapeuticals to diseased sites were an exercise in scientific solitude, and grounds for questioning one's ability to think "like an established scientist". And today we have nanoparticulate paclitaxel as the prime option against metastatic breast cancer, proteomic profiling diagnostic tools based on target surface nanotexturing, nanoparticle contrast agents for all radiological modalities, nanotechnologies embedded in high-distribution laboratory equipment, and no less than 152 novel nanomedical entities in the regulatory pipeline in the US alone.

This is a transforming impact, by any measure, with clear evidence of further acceleration, supported by very vigorous investments by the public and private sectors throughout the world. Even joining the dots in a most conservative, linear fashion, it is easy to envision scenarios of personalized medicine such as the following:

- patient-specific prevention supplanting gross, faceless intervention strategies;
- early detection protocols identifying signs of developing disease at the time when the disease is most easily subdued;
- personally tailored intervention strategies that are so routinely and inexpensively realized, that access to them can be secured by everyone;
- technologies allowing for long lives in the company of disease, as good neighbors, without impairment of the quality of life itself.

These visions will become reality. The contributions from the worlds of small-scale technologies are required to realize them. Invaluable progress towards them was recorded by the very scientists that have joined forces to accomplish the effort presented in this 4-volume collection. It has been a great privilege for me to be at their service, and at the service of the readership, in aiding with its assembly. May I take this opportunity to express my gratitude to all of the contributing Chapter Authors, for their inspired and thorough work. For many of them, writing about the history of their specialty fields of *BioMEMS and Biomedical Nanotechnology* has really been reporting about their personal, individual adventures through scientific discovery and innovation—a sort of family album, with equations, diagrams, bibliographies and charts replacing Holiday pictures . . . .

It has been a particular privilege to work with our Volume Editors: Sangeeta Bhatia, Rashid Bashir, Tejal Desai, Michael Heller, Abraham Lee, Jim Lee, Mihri Ozkan, and Steve Werely. They have been nothing short of outstanding in their dedication, scientific vision, and generosity. My gratitude goes to our Publisher, and in particular to Greg Franklin for his constant support and leadership, and to Angela De Pina for her assistance.

Most importantly, I wish to express my public gratitude in these pages to Paola, for her leadership, professional assistance throughout this effort, her support and her patience. To her, and our children Giacomo, Chiara, Kim, Ilaria and Federica, I dedicate my contribution to BioMEMS and Biomedical Nanotechnology.

With my very best wishes

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Preface

BioMEMS and its extensions into biomedical nanotechnology have tremendous potential both from a research and applications point of view. Exciting strides are being made at intersection of disciplines and BioMEMS and biomedical nanotechnology is certainly one of these very interdisciplinary fields, providing many opportunities of contribution from researchers from many disciplines. In the specific areas of bimolecular sensing, processing and analysis, BioMEMS can play a critical role to provide the various technology platforms for detection of cells, microorganisms, viruses, proteins, DNA, small molecules, etc. and the means to interface the macroscale realm to the nanoscale realm.

We are very pleased to present volume 4 in the Handbook of BioMEMS and Biomedical Nanotechnology, published by Kluwer Academic Press. This volume contains 18 chapters focused on 'Biomolecular Sensing, Processing and Analysis', written by experts in the field of BioMEMS and biomedical nanotechnology. The chapters are groups into three broad categories of Sensors and Materials, Processing and Integrated Systems, and Microfluidics.

Prof. Taun Vo-Dinh from Oakridge National Labs begins the Sensors and Materials section by providing a review of biosensors and biochips. This review is followed by an example of mechanical cantilever sensor work described by Prof. Arun Majumdar's group at UC Berkeley and Prof. Tom Thundat at Oakridge National Laboratory. An example of a nano-scale sensor electrical sensor, an artificial pore, integrated in a microscale device is presented next by Prof. Lydia Sohn's group at UC Berkeley. Cell based sensors are an important class of electrical sensors and Profs. Cengiz Ozkan and Mihri Ozkan at UC Riverside present a review of their work in this area. These chapters on sensors are followed by a review chapter on silicon and glass BioMEMS processing by Prof. Nam Trung Nguyen at Nanyang Technological University. Polymers and hydrogels are an important class of bioMEMS materials and Profs. Nicholas Peppas at UT Austin and Zach Hilt at University of Kentucky provide a review chapter in this area to close off this section.

The Processing and Integrated Systems section is focused on means to manipulate biological and fluidic samples in BioMEMS device and examples of integrated BioMEMS systems. Prof. Abe Lee from UC Irvine presents a review of magnetohydrodynamic methods and their utility in BioMEMS and micro-total-analysis (μTAS) systems. Dielectrophoresis (DEP) is being increasing used at the microscale and in BioMEMS applications and Prof. Joel Voldman from MIT provides a review of DEP and applications, especially for cellular analysis and manipulation. Prof. Rashid Bashir and his group from Purdue present an overview of BioMEMS sensors and devices for cellular sensing, detection and manipulation. Microsystems and BioMEMS integrated with wireless and RF devices for in-vivo applications is a growing field and Prof. Babak Zaiae, previously of University of Minnesota, and now at Purdue, presents an overview of this area. As reviewed in the first section, polymers and hydrogels are a very important class of BioMEMS materials and Prof. David Beebe from University of Wisconsin presents an overview of the work in his group on polymer based self-sensing and actuating microfluidic systems. Lastly, mixing and stirring of fluids is an important problem to be addressed at the microscale due to the fact that Reynold's numbers are small, flows are laminar, and it is challenge to create mixing. Prof. Meinhart and colleagues at UC Santa Barbara present the use of AC electrokinetic methods, including DEP, for mixing of fluids in BioMEMS devices.

The Microfluidics section describes work in a very important supporting field for BioMEMS—microfluidics. Since nearly all life processes occur in or with the help of water, microfluidics is a key technology necessary in miniaturizing biological sensing and processing applications. This section starts off with a contribution by Prof. Steve Wereley's group at Purdue University quantitatively exploring how DEP influences particle motion and proposing a new experimental technique for measuring this influence. Prof. David Erickson from Cornell University and Prof. Dongqing Li from Vanderbilt University have contributed an article reviewing emerging computational methods for simulating flows in microdevices. Prof. Terry Conlisk and Prof. Sherwin Singer's (both of Ohio State University) contribution focused exclusively on modeling electroosmotic flow in nanochannels—a challenging domain where Debye length is comparable to channel dimension. This is followed by a contribution from Prof. Minami Yoda at Georgia Tech describing a new version of the versatile micro-Particle Image Velocimetry technique demonstrating spatial resolutions smaller than 1 micron, a requirement for making measurements in nanochannels. Viosense Corporation, led by Dominique Fourguette, has contributed an article on the development of optical MEMS-based sensors, an area of distinct important to BioMEMS. The last contribution to this section is certainly the most biological. Jennifer McCann together with Profs Thomas Webster and Karen Haberstroh (all of Purdue) have contributed a study of how flow stresses influence vascular cell behavior.

Our sincere thanks to the authors for providing the very informative chapters and to Prof. Mauro Ferrari and Kluwer Academic Press for initiating this project. We hope the text will serve as an excellent reference for a wide ranging audience, from higher level undergraduates and beginning graduate students, to industrial researchers, and faculty members.

With best regards

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