

CONTENTS

<b>1 Introduction</b>	<b>1</b>
Donhee Ham, Hakho Lee and Robert M. Westervelt	

PART I. MICROFLUIDICS FOR ELECTRICAL ENGINEERS

<b>2 Introduction to Fluid Dynamics for Microfluidic Flows</b>	<b>5</b>
Howard A. Stone	
2.1 Introduction.....	5
2.2 Concepts Important to the Description of Fluid Motions .....	9
2.2.1 Basic Properties in the Physics of Fluids.....	9
2.2.2 Viscosity and the Velocity Gradient.....	10
2.2.3 Compressible Fluids and Incompressible Flows .....	11
2.2.4 The Reynolds Number.....	12
2.2.5 Pressure-driven and Shear-driven Flows in Pipes or Channels .....	13
2.3 Electrical Networks and their Fluid Analogs .....	14
2.3.1 Ohm’s and Kirchhoff’s Laws.....	14
2.3.2 Channels in Parallel or in Series.....	16
2.3.3 Resistances in terms of Resistivities, Viscosities and Geometry.....	16
2.4 Basic Fluid Dynamics via the Governing Differential Equations .....	17
2.4.1 Goals.....	17
2.4.2 Continuum Descriptions.....	18
2.4.3 The Continuity and Navier-Stokes Equations .....	19
2.4.4 The Reynolds Number .....	21
2.4.5 Brief Justification for the Incompressibility Assumption .....	22
2.5 Model Flows.....	23
2.5.1 Pressure-driven Flow in a Circular Tube.....	23
2.5.2 Pressure-driven Flow in a Rectangular Channel .....	25
2.6 Conclusions and Outlook .....	28
Acknowledgments .....	28
References .....	29
Author Biography.....	30

<b>3</b>	<b>Micro- and Nanofluidics for Biological Separations</b>	<b>31</b>
	Joshua D. Cross and Harold G. Craighead	
3.1	Introduction .....	31
3.2	Fabrication of Fluidic Structure .....	32
3.3	Biological Applications .....	36
3.4	Microfluidic Experiments .....	40
3.5	Microchannel Capillary Electrophoresis .....	46
3.6	Filled Microfluidic Channels .....	50
3.7	Fabricated Micro- and Nanostructures .....	54
3.7.1	Artificial Sieving Matrices .....	54
3.7.2	Entropic Recoil .....	57
3.7.3	Entropic Trapping .....	61
3.7.4	Asymmetric Potentials .....	65
3.8	Conclusions .....	68
	Acknowledgment .....	69
	References .....	69
	Author biography .....	75
<b>4</b>	<b>CMOS/Microfluidic Hybrid Systems</b>	<b>77</b>
	Hakho Lee, Donhee Ham and Robert M. Westervelt	
4.1	Introduction .....	77
4.2	CMOS/Microfluidic Hybrid System – Concept and Advantages .....	79
4.2.1	Application of CMOS ICs in a Hybrid System .....	80
4.2.2	Advantages of the CMOS/Microfluidic Hybrid Approach .....	82
4.3	Fabrication of Microfluidic Networks for Hybrid Systems .....	84
4.3.1	Direct Patterning of Thick Resins .....	85
4.3.2	Casting of Polymers .....	87
4.3.3	Lamination of Dry Film Resists .....	89
4.3.4	Hot Embossing .....	91
4.4	Packaging of CMOS/Microfluidic Hybrid Systems .....	93
4.4.1	Electrical Connection .....	94
4.4.2	Fluidic Connection .....	94
4.4.3	Temperature Regulation .....	96
4.5	Conclusions and Outlook .....	96
	Acknowledgment .....	97
	References .....	97
	Author Biography .....	100

## PART II. CMOS ACTUATORS

### 5 CMOS-based Magnetic Cell Manipulation System 103

Yong Liu, Hakho Lee, Robert M. Westervelt and Donhee Ham

5.1 Introduction .....	103
5.2 Principle of Magnetic Manipulation of Cells .....	105
5.2.1 Magnetic Beads.....	106
5.2.2 Motion of Magnetic Beads .....	109
5.2.3 Tagging Biological Cells with Magnetic Beads .....	115
5.3 Design of the CMOS IC Chip .....	119
5.3.1 Microcoil Array.....	119
5.3.2 Control Circuitry.....	122
5.3.3 Temperature Sensor .....	128
5.4 Complete Cell Manipulation System .....	129
5.4.1 Fabrication of Microfluidic Channels .....	129
5.4.2 Packaging.....	131
5.5 Experiment Setup.....	131
5.5.1 Temperature Control System .....	132
5.5.2 Control Electronics .....	133
5.5.3 Control Software.....	134
5.6 Demonstration of Magnetic Cell Manipulation System.....	135
5.6.1 Manipulation of Magnetic Beads.....	135
5.6.2 Manipulation of Biological Cells .....	137
5.7 Conclusions and Outlook .....	139
Acknowledgment .....	140
References .....	140
Author Biography.....	142

### 6 Applications of Dielectrophoresis-based Lab-on-a-chip Devices in Pharmaceutical Sciences and Biomedicine 145

Claudio Nastruzzi, Azzurra Tosi, Monica Borgatti, Roberto Guerrieri,  
Gianni Medoro and Roberto Gambari

6.1 General Introduction.....	145
6.1.1 Gene Expression Studies.....	147
6.1.2 Protein Studies .....	147
6.1.3 Quality Assurance and Quality Control (QA/QC) in Pharmaceutical Sciences .....	148
6.2 Dielectrophoresis-based Approaches.....	148

6.3 Dielectrophoresis based Lab-on-a-chip Platforms .....	152
6.3.1 Lab-on-a-chip with Spiral Electrodes.....	152
6.3.2 Lab-on-a-chip with Parallel Electrodes.....	154
6.3.3 Lab-on-a-chip with Two-dimensional Electrode Array.....	155
6.4 Applications of Lab-on-a-chip to Pharmaceutical Sciences .....	155
6.4.1 Microparticles for Lab-on-a-chip Applications.....	155
6.4.2 Microparticles-cell Interactions on Lab-on-a-chip .....	164
6.5 Lab-on-a-chip for Biomedicine and Cellular Biotechnology .....	165
6.5.1 Applications of Lab-on-a-chip for Cell Isolation.....	165
6.5.2 Separation of Cell Populations Exhibiting Different DEP Properties...	166
6.5.3 DEP-based, Marker-Specific Sorting of Rare Cells .....	167
6.6 Future Perspectives: Integrated Sensors for Cell Biology.....	168
6.7 Conclusions .....	171
Acknowledgment .....	172
References .....	172
Author Biography.....	176

## **7 CMOS Electronic Microarrays in Diagnostics and Nanotechnology** **179**

Dalibor Hodko, Paul Swanson, Dietrich Dehlinger, Benjamin Sullivan  
and Michael J. Heller

7.1 Introduction .....	179
7.2 Electronic Microarrays.....	184
7.2.1 Direct Wired Microarrays.....	184
7.2.2 CMOS Microarrays.....	186
7.3 Electronic Transport and Hybridization of DNA.....	190
7.4 Nanofabrication using CMOS Microarrays .....	192
7.4.1 Electric Field Directed Nanoparticle Assembly Process .....	194
7.5 Discussion and Conclusions.....	199
References .....	200
Author Biography.....	205

## **PART III. CMOS ELECTRICAL SENSORS**

## **8 Integrated Microelectrode Arrays** **207**

Flavio Heer and Andreas Hierlemann

8.1 Introduction.....	207
-----------------------	-----

8.1.1 Why using IC or CMOS Technology .....	209
8.2 Fundamentals of Recording of Electrical Cell Activity .....	210
8.2.1 Electrogenic Cells .....	210
8.2.2 Recording and Stimulation Techniques and Tools .....	214
8.3 Integrated CMOS-Based Systems .....	221
8.3.1 High-Density-Recording Devices.....	221
8.3.2 Multiparameter Sensor Chip.....	227
8.3.3 Portable Cell-Based Biosensor .....	228
8.3.4 Wireless Implantable Microsystem .....	231
8.3.5 Fully Integrated Bidirectional 128-Electrode System.....	234
8.4 Measurement Results .....	243
8.4.1 Recordings from Neural and Cardiac Cell Cultures .....	243
8.4.2 Stimulation Artifact Suppression .....	245
8.4.3 Stimulation of Neural and Cardiac Cell Cultures .....	246
8.5 Conclusions and Outlook .....	248
Appendix .....	249
Acknowledgment .....	250
References .....	250
Author Biography.....	257

## **9 CMOS ICs for Brain Implantable Neural Recording**

### **Microsystems** **259**

William R. Patterson III, Yoon-kyu Song, Christopher W. Bull,  
Farah L. Laiwalla, Arto Nurmikko and John P. Donoghue

9.1 Introduction .....	259
9.2 Electrical Microsystem Overview .....	265
9.3 Preamplifier and Multiplexor Integrated Circuit .....	267
9.3.1 Preamplifiers.....	268
9.3.2 Column Multiplexing.....	277
9.3.3 Output Buffer Amplifier .....	278
9.3.4 Biasing and the Bias Generator.....	281
9.3.5 Amplifier Performance.....	283
9.4 Digital Controller Integrated Circuit .....	284
9.5 Conclusions .....	286
Acknowledgment .....	288
References .....	288
Author Biography.....	290

**PART IV. CMOS OPTICAL SENSORS**

**10 Optofluidic Microscope – Fitting a Microscope onto a Sensor Chip** **293**  
Changhui Yang, Xin Heng, Xiquan Cui and Demetri Psaltis

10.1 Introduction .....293

10.2 Operating Principle .....295

10.3 Implementation.....297

    10.3.1 Experimental Setup .....297

    10.3.2 Imaging *C. Elegans* .....299

10.4 Resolution .....302

    10.4.1 Putting Resolution in Context .....302

    10.4.2 Experimental Method.....304

    10.4.3 Simulation Method.....308

    10.4.4 Comparison between Simulation and Experimental Results ..... 310

    10.4.5 Results and Discussions ..... 313

10.5 Resolution and Sensitivity.....320

10.6 OFM Variations .....322

    10.6.1 Fluorescence OFM .....322

    10.6.2 Differential Interference Contrast OFM .....323

10.7 Conclusions.....325

Acknowledgment ..... 326

References .....326

Author Biography.....329

  

**11 CMOS Sensors for Optical Molecular Imaging** **331**  
Abbas El Gamal, Helmy Eltoukhy and Khaled Salama

11.1 Introduction.....331

11.2 Luminescence.....333

    11.2.1 Fluorescence .....333

    11.2.2 Bio-/Chemi-Luminescence .....335

11.3 Solid-State Image Sensors.....336

    11.3.1 Photodetection .....338

    11.3.2 CMOS Architectures.....343

    11.3.3 Non-idealities and Performance Measures .....347

    11.3.4 Sampling Techniques for Noise Reduction .....351

---

11.4 CMOS Image Sensors for Molecular Biology .....	354
11.4.1 CMOS for Fluorometry .....	356
11.4.2 CMOS for Bio-/Chemi-Luminescence.....	357
11.5 Lab-on-Chip for <i>de novo</i> DNA Sequencing.....	357
11.5.1 Lab-on-Chip Application Requirements.....	359
11.5.2. Luminescence Detection System-on-Chip .....	360
11.5.3 Low Light Detection.....	369
11.5.4 Applications.....	372
Acknowledgment .....	374
References .....	374
Author Biography.....	379

<b>Index</b>	<b>381</b>
--------------	------------



<http://www.springer.com/978-0-387-36836-8>

CMOS Biotechnology

Lee, H.; Ham, D.; Westervelt, R.M. (Eds.)

2007, XV, 385 p., Hardcover

ISBN: 978-0-387-36836-8