

Table of Contents

Preface	v
List of Contributors	xix
Chapter 1. Microfluidics: Fundamentals and Engineering Concepts	1
1. Introduction	1
2. Essentials of Fluidic Transport Phenomena at Small Scales	3
2.1. Microflow Versus Macroflow	3
2.2. Nanoflow	8
3. Scaling Analysis	14
3.1. Scaling Analysis for Single-Phase Flow	18
3.1.1. Flow Rate	18
3.1.2. Heat Generation	19
3.1.3. Heat Transfer	20
3.1.4. Mass Transfer and Mixing	22
3.1.5. Hydrodynamic Dispersion	23
3.2. Scaling Analysis for Two-Phase Flow	24
3.2.1. Capillary Filling	25
3.2.2. Droplet Formation	26
3.2.3. Blocking of Channels by Bubbles	27
3.2.4. Particle Trapping by Dipole Forces	29
3.3. Summary of Scaling Laws	31
4. System/Engineering Concepts and Design Approaches for Microfluidics	31
4.1. Engineering Concepts for Microfluidic Systems	31
4.1.1. Mixing	32
4.1.2. Separation	33
4.1.3. Sensing and Detection	34
4.1.4. Pumping	35
4.1.5. Valving	35
4.1.6. Manipulation of Bubbles and Slugs	37
4.1.7. Integration and Materials	38
4.2. Design Methods	42
4.2.1. Reduced Order Models for Single-Phase Flow	43
4.2.2. Multiphase and Particulate Flows	45
4.2.3. Optimization and System Design	48
References	49

Chapter 2. Electrohydrodynamic and Magnetohydrodynamic Micropumps	59
1. Introduction	59
1.1. Basic Features of Conduction in Liquids	60
1.2. Mechanical Aspects of Micropumps	64
2. Electric Forces in the Bulk: Injection, Conduction, and Induction EHD Pumps	66
2.1. Injection Pump	67
2.1.1. Pump Principle	68
2.1.2. Characteristics	72
2.2. Conduction Pump	74
2.2.1. Pump Principle	75
2.2.2. Characteristics	78
2.3. Induction Pump	80
2.3.1. Pump Principle	81
2.3.2. Characteristics	84
3. Electric Forces in the Diffuse Layer: Electroosmotic and AC/IC Electroosmotic Pumps	85
3.1. Electroosmotic Pump	87
3.1.1. Pump Principle	87
3.1.2. Characteristics	90
3.2. AC/IC Electroosmotic Pump	95
3.2.1. Pump Principle	95
3.2.2. Characteristics	98
4. Magnetic Forces: DC and AC MHD Pumps	99
4.1. DC MHD Micropump	100
4.1.1. Pumping Principle	101
4.1.2. Characteristics	102
4.2. AC MHD Micropump	104
4.2.1. Pump Principle	105
4.2.2. Characteristics	106
5. Comparisons and Conclusions	107
References	111
Chapter 3. Mixing in Microscale	117
1. Introduction	117
2. Mass Transport in Microscale	118
2.1. Transport Effects	118
2.1.1. Diffusive Transport	118
2.1.2. Advective Transport	119
2.1.3. Taylor–Aris Dispersion	120
2.1.4. Chaotic Advection	120
2.2. Dimensionless Numbers and Scaling Laws	121

3. Micromixers Based on Molecular Diffusion	125
3.1. Parallel Lamination	125
3.1.1. Mixers Based on Pure Molecular Diffusion	125
3.1.2. Mixers Based on Inertial Instabilities	128
3.2. Sequential Lamination	129
3.3. Sequential Segmentation	130
3.4. Segmentation Based on Injection	133
3.5. Focusing of Mixing Streams	136
4. Micromixers Based on Chaotic Advection	139
4.1. Chaotic Advection in a Continuous Flow	139
4.1.1. Chaotic Advection at High Reynolds Numbers	140
4.1.2. Chaotic Advection at Intermediate Reynolds Numbers	142
4.1.3. Chaotic Advection at Low Reynolds Numbers	142
4.2. Chaotic Advection in Multiphase Flow	143
5. Active Micromixers	146
5.1. Pressure-Driven Disturbance	146
5.2. Electrohydrodynamic Disturbance	147
5.3. Dielectrophoretic Disturbance	147
5.4. Electrokinetic Disturbance	148
5.5. Magnetohydrodynamic Disturbance	148
5.6. Acoustic Disturbance	148
5.7. Thermal Disturbance	149
References	149
Chapter 4. Control of Liquids by Surface Energies	157
1. Introduction	157
2. Capillary Model	159
2.1. Equilibrium Conditions	160
2.2. Contact Line Pinning	162
2.3. Computation of Droplet Shapes	163
3. Plane Substrates with Wettability Patterns	164
3.1. Experimental	165
3.2. Circular Surface Domains	167
3.2.1. Array of Hydrophilic Discs	168
3.2.2. Array of Hydrophobic Discs	170
3.3. Striped Surface Domains	171
3.3.1. Perfectly Wettable Stripe	171
3.3.2. Partially Wettable Stripe	173
3.3.3. Hydrophilic Rings	176
3.3.4. Liquid Wetting Several Stripes	178

4. Wetting of Topographically Patterned Substrates	181
4.1. Substrate Preparation	182
4.2. Basic Topographies: Infinite Wedge and Step	184
4.2.1. Infinite Wedge	184
4.2.2. Tip Shape	185
4.2.3. Topographic Step	186
4.3. Triangular Grooves	187
4.4. Rectangular Grooves	190
4.5. Switching Equilibrium Morphologies	194
5. Summary and Outlook	196
References	197
Chapter 5. Electrowetting: Thermodynamic Foundation and Application to Microdevices	203
1. Introduction	203
2. Theoretical Background	205
2.1. Surface Tension	205
2.2. Surface Thermodynamics	206
2.3. General Concept of Work	208
2.4. Surface Tension in Thermodynamic Consideration	208
2.5. Liquid–Liquid and Liquid–Solid Interfaces: Young’s Equation	209
2.6. Pressure Difference at the Curvilinear Surface	211
2.6.1. Example: Application of the Laplace-Young Equation	213
2.7. Control of Surface Tension	214
2.7.1. Example 1: Chemical Potential – Surface Tension System	215
2.7.2. Example 2: Temperature – Surface Tension System	217
2.7.3. Example 3: Electric Potential – Surface Tension System	218
3. Electrowetting and Its Recent Variations	220
3.1. Electric Double Layer	220
3.2. Electrocapillarity: Lippmann’s Experiment	221
3.3. Electrowetting: On Solid Electrode	223
3.4. Electrowetting: On Dielectric	224
4. Microfluidic Device Using Electrowetting	227
4.1. Pumping by Electrowetting on Liquid Electrode: CEW	227
4.2. Pumping by Electrowetting on Solid Electrode	228
4.3. Pumping by Electrowetting on Dielectric-Coated Solid Electrode (EWOD)	229
4.4. Reconfigurable Digital (or Droplet) Microfluidics	234

5. Summary	236
References	236
Chapter 6. Magnetic Beads in Microfluidic Systems – Towards New Analytical Applications	241
1. Introduction	241
2. Types of Magnetic Beads	242
3. Forces on Magnetic Beads	244
4. Magnetic Bead Separation	246
5. Magnetic Bead Transport	250
6. Magnetic Beads as Labels for Detection	253
7. Separation and Mixing Using Magnetic Supraparticle Structures	257
8. Magnetic Beads as Substrates for Bio-assays	258
9. Magnetic Beads in Droplets	262
10. Conclusion	265
References	266
Chapter 7. Manipulation of Microobjects by Optical Tweezers	275
1. Introduction	275
2. Single-Particle Manipulation with a Focused Laser Beam	276
2.1. Trapping of a Micro/nano Particle with a Focused Laser Beam	276
2.2. Trapping of a Metallic Particle	279
2.3. Rotation of a Birefringent Microparticle	281
2.4. Manipulation of a Micromachined Object	283
3. Multiparticle Manipulation Techniques	288
3.1. Single Beam Based Manipulation	288
3.1.1. Time-Divided Laser Scanning for the Manipulation of Multiple Microparticles	288
3.1.2. Continuous Transportation of Multiple Particles	289
3.1.3. Bessel Beam for the Manipulation of Multiple Particles	290
3.2. Holographic Optical Tweezers	292
3.3. Evanescent Waves for the Propulsion of Microparticles	295
4. Optically Driven Microfluidic Components	297
4.1. Particle Sorter Using an Optical Lattice	297
4.2. Optically Driven Micropump and Microvalve with Colloidal Structures	299
4.3. Optically Driven Micropump Produced by Two-Photon Microstereolithography	301
4.4. Optically Controlled Micromanipulators Produced by Two-Photon Microstereolithography	303

5. Bio-manipulation Based on Optical Tweezers	305
5.1. Cell Stretcher Using Optical Radiation Pressure	305
5.2. Manipulation of Biomolecules with Optically Trapped Micro/nano Particles	306
5.3. Optically Controlled Microtools for Biological Samples	308
6. Conclusions and Outlook	309
References	309
Chapter 8. Dielectrophoretic Microfluidics	315
1. Introduction	315
2. Quantification of Dielectrophoretic Micro-Fluidics	316
2.1. Electric Force Acting on an Individual Particle	316
2.2. Field Driven Phase Transitions	320
2.3. Electro-Hydrodynamic Models	323
2.3.1. Single-Particle Model	323
2.3.2. Model for Collective Phenomena	325
3. Microfluidic Applications of Dielectrophoresis	329
3.1. Primary Flows	330
3.2. Non-uniform Electric Field Generators	331
3.3. Modes of Operation	332
3.4. Depletion and Enhancement	335
3.5. Architectural Considerations	337
3.5.1. Fouling	337
3.5.2. Throughput	338
3.5.3. Concentration Factor	340
3.5.4. Heating	342
3.6. Examples of Architectures	343
3.6.1. Post-Based Devices	343
3.6.2. Facet-Based Devices	344
3.6.3. Corduroy Devices	347
4. Conclusion	350
References	351
Chapter 9. Ultrasonic Particle Manipulation	357
1. Introduction	357
2. Theory	358
2.1. Radiation Forces	358
2.1.1. Radiation Forces on Small Compressible and Incompressible Spheres	358
2.1.2. Some Practical Considerations	362
2.1.3. Lateral Forces and Secondary Radiation Forces	363

2.2. Acoustic Streaming	364
2.3. Modelling of Standing Waves for Ultrasonic Force Fields	365
2.4. Field Modelling	365
3. Transduction Techniques	368
3.1. Direct Excitation of Bulk Acoustic Waves	368
3.1.1. Bulk PZT	369
3.1.2. Thick-Film PZT	370
3.2. Magnetostrictive Excitation	371
3.3. Excitation via Leaky Surface Waves and Plate Waves	372
3.4. Sol–Gel	372
3.5. Alternative Materials	373
4. Applications of Ultrasonic Particle Manipulation	373
4.1. Cell Viability	374
4.2. Filtration and Concentration	374
4.2.1. Enhanced Sedimentation	374
4.2.2. Flow-Through Filtration	375
4.2.3. Ultrasound Within a Porous Mesh	377
4.3. Particle Trapping	377
4.3.1. Trapping to Enhance Particle–Particle Interaction	378
4.3.2. Trapping to Enhance Particle–Fluid Interaction	378
4.4. Sensor Enhancement	379
4.5. Particle Washing – Exchange of Containing Medium	380
4.6. Particle Fractionation	381
5. The Future of Ultrasonic Particle Manipulation	383
References	383
Chapter 10. Electrophoresis in Microfluidic Systems	393
1. Introduction	393
1.1. Free Solution Electrophoresis	395
1.2. Gel Electrophoresis	395
1.3. Isoelectric Focusing (IEF)	396
1.4. Micellar Electrokinetic Chromatography (MEKC)	396
2. Electrophoresis in Microfabricated Systems	396
2.1. Injection and Separation	398
2.2. Sieving Gels	401
2.3. Detection	402
2.4. Device Construction	404
3. Applications of Microchip Electrophoresis	407
3.1. Advanced Electrophoresis Methods	409
3.2. Integrated Systems	411
4. Summary and Outlook	414
References	415

Chapter 11. Chromatography in Microstructures	439
1. Introduction	439
1.1. Background	439
1.2. Short Overview of Some Variants of Chromatography	441
1.2.1. Gas Chromatography (GC)	441
1.2.2. Pressure-Driven Liquid Chromatography (LC)	441
1.2.3. Electrochromatography (EC)	442
1.2.4. Miscellaneous	442
1.3. Some Theoretical Considerations	443
2. Examples of Chromatography on Microchips	445
2.1. Gas Chromatography (GC)	445
2.2. Pressure-Driven Liquid Chromatography (LC)	449
2.3. Capillary Electrochromatography (CEC)	454
2.4. Other Chromatographic Methods on Microchips	463
3. Conclusions	465
References	466
Chapter 12. Microscale Field-Flow Fractionation: Theory and Practice	471
1. Introduction	471
2. Background and Theory	472
2.1. FFF Operating Modes and SPLITT Fractionation	473
2.2. FFF Retention Theory	475
2.3. Plate Height	477
2.3.1. Nonequilibrium Plate Height	479
2.3.2. Instrumental Plate Height	479
2.4. Resolution	479
3. Miniaturization Effects in FFF	480
3.1. Instrumental Plate Height	480
3.2. Gradient-Based Systems	481
3.2.1. Plate Height Scaling	481
3.2.2. Resolution Scaling	482
3.3. Nongradient-Based Systems	483
3.3.1. Plate Height Scaling	483
4. Microscale Electrical FFF	485
4.1. Theory	486
4.2. Fabrication and Packaging	489
4.3. System Characteristics	490
4.3.1. Retention	491
4.3.2. Separations	492
4.3.3. Effective Field Scaling	493
5. Microscale Cyclical Electrical FFF	494
5.1. Theory	495

5.1.1. Effective Field Model	496
5.1.2. Steric Effects in CyFFF	497
5.1.3. Particle Diffusion Effects	497
5.2. Experimental Results	498
5.2.1. Comparison of Theory with Experimental Data	498
5.2.2. Separations	499
5.2.3. Effects of Carrier pH and Ionic Strength	500
6. Microscale Dielectrophoretic FFF	501
6.1. Theory	501
6.2. Experimental Results	504
7. Microscale Thermal FFF	505
8. Miniaturized Flow FFF	507
9. Microscale Acoustic FFF	508
10. Other Microscale FFF Efforts	509
10.1. Microscale Split-Flow Thin Fractionation	510
10.2. Microscale Hydrodynamic Chromatography	511
11. Nanoscale FFF	513
12. Conclusion	515
References	516
Chapter 13. Nucleic Acid Amplification in Microsystems	523
1. General Elements of Amplification	523
2. Micro–Macro Comparison	526
2.1. Typical Length Scales	526
2.2. Volumetric Effects	527
2.3. Surface Effects	528
2.4. Linear, Timescale and Other Effects	529
3. Microfluidic Realization Methods	530
3.1. Substrates	531
3.2. Types of Setup	532
3.2.1. Amplification in Wells	533
3.2.2. Amplification by Continuous Flow-Through Devices	536
3.2.3. Special Realization Methods	538
3.3. Surface Treatments	543
3.4. Detection of Amplified DNA	546
3.5. Integrated Micro-PCR Systems	547
4. Alternative Protocols to PCR	551
5. Conclusion	554
References	555

Chapter 14. Cytometry on Microfluidic Chips	569
1. Introduction	569
2. Design of Microfluidic Flow Cytometers	572
2.1. Transport and Focusing of Cell Suspensions	572
2.2. The Sorting Unit: Active Microfluidic Switches	574
2.3. Integration of Several Functionalities on Microchips	579
3. Detection Concepts for Ultrasensitive Cytometry	580
3.1. Single Molecule Fluorescence Spectroscopy in Microfluidic Channels	580
3.2. Determination of Flow Velocity by Fluorescence Correlation Spectroscopy (FCS)	586
3.3. Integration of Optical Components into Microfluidic Chips	590
3.4. Other Detection Techniques	590
4. Perspectives for Biotechnology	592
4.1. Sorting of Single Molecules	592
4.2. Cell-Free Protein Expression in Microfluidic Chips	593
4.3. Perspectives of Generating Membrane Vesicles in Microstructures	596
5. Conclusion	598
References	598
Index	607