

Contents

Preface xv

1 Fundamentals of Acoustic Wave Generation and Propagation 1

Mehmet A. Sahin, Mushtaq Ali, Jinsoo Park, and Ghulam Destgeer

- 1.1 Introduction 1
- 1.1.1 Acoustic or Sound Waves 1
- 1.1.2 Dominos Effect 1
- 1.1.3 Elastic vs Inelastic Waves 2
- 1.1.4 Scope of Acoustics 4
- 1.2 Brief History of Acoustic Waves 4
- 1.2.1 Early History 4
- 1.2.2 History of Acoustic Streaming 4
- 1.2.3 History of Acoustic Radiation Force 5
- 1.3 What Is an Acoustic Wave? 6
- 1.3.1 Acoustic Parameters 6
- 1.3.2 Displacement, Velocity, and Pressure Fields 6
- 1.3.3 Wave Propagation 7
- 1.3.4 Wave Dissipation 7
- 1.3.5 Wave Dispersion 8
- 1.4 Modes of Acoustic Waves 8
- 1.4.1 Categorization Based on Frequency Range 9
- 1.4.2 Categorization Based on Propagation Mode 9
- 1.4.2.1 Longitudinal Waves 9
- 1.4.2.2 Shear Waves 10
- 1.4.2.3 Rayleigh Waves 11
- 1.4.2.4 Love Waves 12
- 1.4.2.5 Lamb Waves 12
- 1.4.3 Categorization Based on Wave Configuration 12
- 1.4.3.1 Traveling Waves 12
- 1.4.3.2 Standing Waves 13
- 1.5 Acoustic Wave Propagation and Interaction 13
- 1.5.1 Transmission and Reflection of Acoustic Waves 13

1.5.2	Acoustic Scattering	14
1.5.3	Acoustic Radiation	16
1.6	Acoustic Wave Attenuation	18
1.6.1	Viscoelastic Attenuation	18
1.6.2	Acousto-Thermal Heating	19
1.6.3	Acoustic Streaming Flow	19
1.6.3.1	Eckart Streaming	20
1.6.3.2	Rayleigh Streaming	20
1.6.3.3	Bubble-Driven Microstreaming	21
1.6.3.4	Applications of Acoustic Streaming Flow	21
1.7	Generation and Propagation of Acoustic Waves	22
1.7.1	Acoustic Waves Generation in Nature	22
1.7.2	Generation of Acoustic Waves in Lab	22
1.7.2.1	Lower-Frequency Acoustic Waves	22
1.7.2.2	Piezoelectricity and High-Frequency Wave Generation	23
1.8	Acoustic Waves Effects in Fluidic Media	24
1.8.1	Vibrating Membranes and Sharp-Edge Structures	25
1.8.2	Oscillating Bubbles	25
1.8.2.1	Cavitation	26
1.8.3	Optoacoustic Imaging	27
1.8.4	Manifestations of Acoustic Radiation Force and Acoustic Streaming Flow	28
	List of Abbreviations and Symbols	28
	References	29
2	Basic Theories and Physics of Acoustic Technologies	37
	<i>Khemraj G. Kshetri and Nitesh Nama</i>	
2.1	Introduction	37
2.2	Acoustic Waves in Solids	38
2.2.1	Governing Equation	39
2.2.2	Acoustic Waves in Non-piezoelectric Solids	39
2.2.3	Acoustic Waves in Piezoelectric Solids	40
2.3	Acoustic Waves in Fluids	40
2.3.1	Governing Equations	40
2.3.2	Acoustic Streaming	41
2.3.2.1	Modeling Approach for Slow Streaming	44
2.3.2.2	Modeling Approach for Fast Streaming	45
2.3.3	Distinction Between Lagrangian and Eulerian Fluid Velocity and Stokes' Drift	46
2.3.4	Acoustic Streaming Near Solid Particles	47
2.3.5	Acoustic Streaming Near Fluid–Fluid Interfaces	47
2.4	Forces in Acoustofluidic Systems	49
2.4.1	Primary Acoustic Radiation Force	49
2.4.2	Secondary Acoustic Radiation Force	52
2.4.2.1	Forces Between Two Rigid Spheres	53

2.4.2.2	Forces Between Two Bubbles	53
2.4.2.3	Forces Between a Solid Particle and a Bubble	54
2.4.2.4	Forces Between a Liquid Drop and a Bubble	55
2.4.3	Hydrodynamic Drag Force	55
2.5	Conclusions and Perspectives	57
	References	58

3 Materials for Acoustic Wave Generation and Modulation 67

Noé Jiménez

3.1	Introduction	67
3.1.1	Generation and Detection of Ultrasound	67
3.1.2	Technologies for Ultrasound Transducers	68
3.2	Piezoelectricity	68
3.2.1	Model Equations	68
3.2.1.1	Stress-Charge Formulation	69
3.2.1.2	Strain-Charge Formulation	70
3.2.1.3	Stress-Field Formulation	70
3.2.1.4	Strain-Field Formulation	70
3.2.2	The Piezoelectric Constants	70
3.2.3	Longitudinal Motion in a Piezoelectric Material	71
3.2.3.1	A Simple Piezoelectric Model	71
3.2.3.2	Waves in the Piezoelectric Material	72
3.3	Piezoelectric Materials	73
3.3.1	Piezoelectric Crystals	73
3.3.2	Piezoelectric Ceramics	74
3.3.3	Piezoelectric Polymers	74
3.3.4	Piezoelectric Composites	74
3.4	Ultrasound Transducers	75
3.4.1	Elements of a Transducer	75
3.4.2	The Piezoelectric Slab	75
3.4.3	Matching Layers	76
3.4.3.1	Classical Matching Layer Design	76
3.4.3.2	Multiple Matching Layer Design	77
3.4.3.3	Broadband Matching Layer Design	77
3.4.4	Backing Layer	77
3.4.5	Electrical Impedance Matching Network	78
3.5	Ultrasound Beams	78
3.5.1	Circular Aperture Transducers	78
3.5.2	Focused Transducers	80
3.5.3	Phased-Array Transducers	83
3.6	Acoustic Lenses	83
3.6.1	Refraction by Bulky Lenses	84
3.6.1.1	Spherical Lenses	84
3.6.1.2	Ellipsoidal Lenses	85
3.6.1.3	Axicon Lenses	85

3.6.1.4	Fresnel and Fraxicon Lenses	86
3.6.1.5	Lenses for Vortex Generation	86
3.6.2	Diffraction by Gratings	87
3.6.2.1	Cartesian Diffraction Grating	87
3.6.2.2	Asymmetric Diffraction Grating	87
3.6.2.3	Fresnel Zone Plates	88
3.6.2.4	Archimedean Spiral Gratings	89
3.6.2.5	Fresnel-Spiral Zone Plate	90
3.6.3	Reflection by Curved Surfaces	90
3.6.3.1	Parabolic Reflectors	91
3.6.3.2	Ellipsoidal Reflectors	91
3.6.4	Holograms	91
3.6.4.1	Field Projections	91
3.6.4.2	Synthesis of Acoustic Images	93
3.6.4.3	Biomedical Applications of Holograms	94
	References	95

4 Ultrasound and Ultrasonic Imaging in Medicine: Recent Advances 99

Tuğba Ö. Onur

4.1	Introduction	99
4.2	Ultrasound Waves	99
4.2.1	Types of Ultrasonic Waves	100
4.2.2	Behavior of Ultrasound Waves at Interfaces	100
4.2.3	Ultrasound Power and Intensity	101
4.2.4	Ultrasound Applications	102
4.3	Ultrasonic Imaging	103
4.3.1	Ultrasonic Imaging System	106
4.3.1.1	Transducer	106
4.3.1.2	Probes	107
4.3.1.3	Central Processing Unit	109
4.3.1.4	Output Display	109
4.3.2	Focus	109
4.3.3	Resolution	109
4.3.4	Beamforming	110
4.4	Sound-Tissue Interactions in Ultrasonography	110
4.4.1	Reflection	110
4.4.2	Refraction	111
4.4.3	Absorption	112
4.4.4	Attenuation	112
4.4.4.1	Attenuation by Reflection, Refraction, and Deflection	112
4.4.4.2	Attenuation by Scattering	113
4.4.4.3	Attenuation by Absorption	113
4.4.4.4	Time Gain Reduction (TGR) and Depth Gain Reduction (DGR)	114
4.5	Ultrasonic Imaging Methods	114

4.5.1	Real-Time Imaging	114
4.5.1.1	A-Mode	115
4.5.1.2	M-Mode	116
4.5.1.3	B-Mode	117
4.5.2	Doppler Ultrasonography	118
4.5.2.1	Continuous Wave Doppler	119
4.5.2.2	Duplex Doppler	119
4.5.2.3	Color Doppler	119
4.5.3	Real-Time Artifacts in Imaging	119
4.5.4	Factors Affecting Image Quality	120
4.6	Tissue Harmonic Imaging (THI)	121
4.6.1	The Occurrence of Harmonic Signals	121
4.6.2	The Separation of Harmonic Signals from the Main Signal	122
4.6.3	The Advantages of Harmonic Signals	122
4.7	Recent Advances in Ultrasound Imaging for Medicine	122
	References	123

5 Photoacoustic Imaging and Sensing for Biomedical Applications 127

Amalina B. E. Attia, Ruochong Zhang, Mohesh Moothanchery, and Malini Olivo

5.1	Introduction	127
5.2	Photoacoustic Imaging Applications	130
5.2.1	PAI of Breast Cancer	130
5.2.1.1	In Vivo Imaging	130
5.2.1.2	Ex Vivo Imaging	132
5.2.2	PAI for Skin Imaging	133
5.2.2.1	PAI of Skin Cancer	135
5.2.2.2	PAI of Inflammatory Skin Diseases	137
5.2.2.3	PAI of Wounds	137
5.3	Photoacoustic Sensing for Biomedical Applications	139
5.3.1	Noninvasive Temperature Monitoring in Deep Tissue	139
5.3.2	Noninvasive Glucose Sensing	142
	References	148

6 Therapeutic Ultrasound 159

Bar Glickstein, Hila Shinar, and Tali Illovitsh

6.1	Introduction	159
6.2	Ultrasound-Induced Bioeffects	160
6.2.1	Introduction	160
6.2.2	Thermal Effects	160
6.2.3	Mechanical Effects	161
6.2.3.1	Cavitation	161
6.2.4	Contrast-Enhanced Effects	161
6.2.4.1	Microbubbles	161

6.2.4.2	Nanobubbles	162
6.2.4.3	Nanodroplets	162
6.2.5	Safety and Regulations	163
6.3	Therapeutic Ultrasound Applications	164
6.3.1	High-Intensity Focused Ultrasound	164
6.3.2	Histotripsy	166
6.3.3	Shock Wave Lithotripsy	169
6.3.4	Drug Delivery and Gene Therapy	170
6.3.5	Blood–Brain Barrier Opening	171
6.3.6	Low-Intensity Ultrasound for Neuromodulation	172
6.3.7	Bone Healing	172
6.3.8	Sonothrombolysis	172
6.3.9	Other Applications	173
6.4	Conclusions	173
	References	174
7	Application of Ultrasound-Responsive Reagents for Drug Delivery Systems	181
	<i>Hiroshi Kida and Katsuro Tachibana</i>	
7.1	Historical Background of Research on Bubble Reagents for Medicine	181
7.2	Use of Bubble Reagents as Drug Delivery Systems	182
7.2.1	Acoustic Cavitation	182
7.2.2	Importance of Inertial and Non-inertial Cavitation in Improving Drug Permeability	184
7.2.3	Targeting and Focusing Using Acoustic Means	186
7.3	Variation of Ultrasound-Responsive Reagents for DDS	186
7.3.1	Shell Composition	186
7.3.2	Improved Stability by Polyethylene Glycol (PEG) Modification	187
7.3.3	Modification with Targeting Ligands	188
7.3.4	Drug and Gene Loading	188
7.3.5	Extended Adaptation of Ultrasound-Responsive Reagents	190
7.4	Research on Treatment of Diseases Using Ultrasonic Drug Delivery	192
7.4.1	Cancer	192
7.4.2	Central Nervous System Diseases	195
7.5	Conclusion	197
	References	198
8	Acoustic Levitation and Acoustic Holograms	217
	<i>Tatsuki Fushimi and Yoichi Ochiai</i>	
8.1	Introduction	217
8.1.1	History of Acoustic Levitation	217
8.1.1.1	Classical Acoustic Levitator	218
8.1.1.2	Phased Array Levitator (PAL)	221
8.2	Acoustic Holograms	224

8.3	Numerical Simulation of Acoustic Levitator	227
8.3.1	Pressure Field Calculation	227
8.3.1.1	Huygens' Approach	227
8.3.1.2	Spherical Harmonics Expansion	228
8.3.1.3	Angular Spectrum Method	229
8.3.2	Acoustic Radiation Force	230
8.3.2.1	Gor'kov	230
8.3.2.2	Spherical Harmonic Approach	231
8.4	Acoustic Hologram Optimization	231
8.4.1	Optimization Example with Diff-PAT	233
8.5	Applications in Biology and Medicine	234
8.5.1	Specimen Holding	234
8.5.2	Experiment Automation	234
8.5.3	3D Display	235
8.6	Conclusion and Future Remarks	236
	Acknowledgments	237
	References	237
9	Application of Ultrasonic Waves in Bioparticle Manipulation and Separation	243
	<i>M. Bülent Özer and Barbaros Çetin</i>	
9.1	Introduction	243
9.2	Bioparticle Manipulation	244
9.2.1	Hydrodynamic Bioparticle Manipulation	244
9.2.2	Immunological (Antigen–Antibody Reaction) Bioparticle Manipulation	245
9.2.3	Electrokinetic Bioparticle Manipulation	245
9.2.4	Magnetophoretic Bioparticle Manipulation	245
9.2.5	Acoustophoretic Bioparticle Manipulation	246
9.2.6	Unification of Field Manipulation Methods	246
9.2.7	Comparison of Bioparticle Manipulation Methods	248
9.3	General Architecture of Acoustofluidic Devices	249
9.3.1	BAW Device Architecture	249
9.3.1.1	Piezoelectric Actuator	249
9.3.1.2	Chip Material	250
9.3.1.3	Lid Material	251
9.3.1.4	Device Assembly and Critical Dimensions	251
9.3.2	SAW Device Architecture	252
9.3.2.1	Piezoelectric Actuator	252
9.3.2.2	Interdigital Electrodes (IDT)	253
9.3.2.3	Microfluidic Chamber	254
9.3.2.4	Device Assembly and Critical Dimensions	254
9.3.3	Comparison of BAW and SAW Devices	254
9.4	Governing Equations in Acoustic Bioparticle Manipulation	255
9.4.1	First-Order Acoustic Field Variables	255

9.4.2	Second-Order Acoustic Field Variables	257
9.4.3	Acoustic Radiation Force on a Particle	258
9.4.4	Acoustic Radiation Force on a Particle Considering the Effect of Chip Material	260
9.5	Simulation of Acoustophoretic Bio-Particle Manipulation	264
9.5.1	Simulation of Piezoelectric Actuators	264
9.5.2	Numerical Simulations of the Elastic Material Surrounding the Channel	265
9.5.3	Simulation of Fluid Flow	266
9.5.4	Simulation of Particle Motion	267
9.6	Acoustofluidic Devices in Biological and Medical Applications	269
9.6.1	Applications Regarding Lipid Particles	269
9.6.2	Applications Regarding Cell Wash	278
9.6.3	Applications Regarding Separation of Blood Components	279
9.6.3.1	Plasma Separation	279
9.6.3.2	Platelet Separation	279
9.6.3.3	Separation of WBCs	280
9.6.4	Applications Regarding Cancer Cells	281
9.6.5	Applications Regarding Miscellaneous Cells	282
9.6.6	Application Regarding Bacteria	284
9.6.7	Applications Regarding Nanoscale (Bio)Particles	287
9.6.8	Miscellaneous Applications	289
9.7	Commercial and Regulatory Considerations for Acoustofluidic Devices	290
9.7.1	Cost	291
9.7.2	High Volume Manufacturing	292
9.7.3	Sterilization	292
9.7.4	Biocompatibility	294
9.7.5	Storage and Transportation Requirements	294
9.8	Summary and Outlook	294
	References	296
10	Acoustic Biosensors	305
	<i>Alper Sışman, Paddy French, Ayşe Ogan, Erdal Korkmaz, Abbas A. Husseini, Ali M. Yazdani, and Johan Meyer</i>	
10.1	Introduction	305
10.1.1	Bulk Acoustic Wave (BAW) Mode	305
10.1.2	Surface Guided Acoustic Wave (SGAW) Modes	307
10.2	Biochemical Fundamentals of Sensing	310
10.2.1	Immobilization Strategies of Detection Element	311
10.2.1.1	Noncovalent Immobilization	311
10.2.1.2	Covalent Immobilization	312
10.2.1.3	Bioaffinity Bindings	313
10.3	Bulk Acoustic Wave Biosensors	314
10.3.1	Quartz Microbalance (QMB) Crystal Biosensors	315

10.3.2	Film Bulk Acoustic Wave (FBAR) Biosensors	316
10.4	Surface Transverse Wave Biosensors	317
10.4.1	SH-Wave and Love Wave Biosensors	317
10.4.2	Lamb Waves Biosensors	321
10.4.3	Rayleigh Wave Biosensors	324
10.4.4	Crystal Cuts and Axis Orientation	325
10.5	Commercial Biosensors and Trends	327
10.6	Conclusion	331
	References	332
11	Acoustic Micro/Nanorobots in Medicine	343
	<i>Murat Kaynak, Amit Dolev, and Mahmut S. Sakar</i>	
11.1	Introduction	343
11.2	Theoretical Background	345
11.2.1	Introduction to Acoustics	345
11.2.2	Time-Averaged Acoustically Induced Forces	348
11.2.2.1	Primary Radiation Forces	348
11.2.2.2	Secondary Radiation Forces	351
11.2.2.3	Drag and Thrust-Induced Acoustic Streaming	354
11.3	Acoustic Micromanipulation Techniques	355
11.3.1	Introduction to Acoustic Tweezers	356
11.3.2	Acoustic Micromanipulation Using Bulk Acoustic Waves	357
11.4	Micro/Nanorobotic Devices Actuated by Acoustic Fields	361
11.4.1	Mobile Acoustic Micromachines	361
11.4.2	Soft Robotic Microsystems	363
11.5	In Vivo Actuation of Micro/Nanorobotic Devices	365
11.6	Discussion and Outlook	367
	Acknowledgment	368
	References	368
	Index	375