

<b>Contents</b>		
1	Introduction . . . . .	1
1.1	Biological Micromanipulation . . . . .	1
1.2	Tethered Micromachines for Bio-micromanipulation . . . . .	2
1.3	Untethered Micromachines for Bio-micromanipulation . . . . .	5
1.4	Lab-on-a-Chip Micromachines for Bio-micromanipulation . . . . .	6
1.5	Microscopes for Biological Micromanipulation . . . . .	7
1.6	Microforce Sensing and Feedback Control . . . . .	8
1.7	Conclusion . . . . .	9
	References . . . . .	10
<b>2</b>	<b>Review of Microinjection Systems . . . . .</b>	<b>15</b>
2.1	Introduction . . . . .	15
2.1.1	The Role of Cell Microinjection . . . . .	15
2.1.2	Conventional Manual Cell Microinjection . . . . .	16
2.1.3	Current Methods of Cell Microinjection . . . . .	17
2.2	Injection of Adherent Cells . . . . .	18
2.3	Injection of Suspended Cells . . . . .	20
2.3.1	Drosophila Melanogaster Embryo . . . . .	20
2.3.2	Zebrafish Embryo . . . . .	21
2.3.3	Mouse Embryo . . . . .	22
2.4	Robotic Cell Microinjection System . . . . .	22
2.5	Microforce Sensors for Cell Microinjection . . . . .	24
2.5.1	Vision-Based Force Sensors . . . . .	25
2.5.2	Capacitive Force Sensors . . . . .	29
2.5.3	Optical-Based Force Sensors . . . . .	30
2.5.4	Piezoresistive Force Sensors . . . . .	32
2.5.5	Piezoelectric Force Sensors . . . . .	34
2.6	Current Challenges on Cell Microinjection . . . . .	36
2.6.1	Micromanipulator Design . . . . .	36
2.6.2	Injection Control Design . . . . .	37

2.6.3	Cell Holder Design . . . . .	37
2.6.4	Penetration Scheme Design . . . . .	39
2.6.5	Injecting Pipette Maintenance . . . . .	40
2.6.6	Injection Volume Issue . . . . .	40
2.7	Conclusion . . . . .	41
	References . . . . .	42
<b>3</b>	<b>Design, Fabrication, and Testing of a Microforce Sensor for Microinjection . . . . .</b>	<b>49</b>
3.1	Introduction . . . . .	49
3.2	Mechanism Design of the Microforce Sensor . . . . .	51
3.3	Modeling of the Microforce Sensor . . . . .	53
3.4	Fabrication and Calibration of the Microforce Sensor . . . . .	55
3.4.1	Experimental Setup . . . . .	55
3.4.2	Calibration Results . . . . .	56
3.5	Application in Cell Microinjection . . . . .	59
3.5.1	Experimental Setup . . . . .	60
3.5.2	Results and Discussions . . . . .	62
3.6	Conclusion . . . . .	63
	References . . . . .	63
<b>4</b>	<b>Design and Control of a Piezoelectric-Driven Microinjector . . . . .</b>	<b>65</b>
4.1	Introduction . . . . .	65
4.2	Mechanism Design of the Piezo-Driven Cell Microinjector . . . . .	66
4.3	Prototype Fabrication and Calibration . . . . .	68
4.3.1	Prototype Fabrication and Experimental Setup . . . . .	69
4.3.2	Calibration of Position Sensor . . . . .	71
4.3.3	Calibration of Force Sensor . . . . .	72
4.4	Preliminary Experimental Study . . . . .	73
4.4.1	Position and Force Controller Design . . . . .	73
4.4.2	Motion Planning for Cell Microinjection . . . . .	74
4.4.3	Experimental Study of Cell Microinjection . . . . .	75
4.5	Advanced Position and Force Switching Control Design . . . . .	79
4.5.1	Weight-Based Switching Control System . . . . .	79
4.5.2	Adaptive Sliding Mode Position Controller Design . . . . .	81
4.5.3	Incremental PID Force Controller Design . . . . .	84
4.5.4	Switching Scheme Design . . . . .	84
4.6	Experimental Testing Results . . . . .	85
4.6.1	Controller Setup . . . . .	85
4.6.2	Position/Force Switching Control Results . . . . .	86
4.6.3	Discussions . . . . .	88
4.7	Conclusion . . . . .	89
	References . . . . .	89

<b>5 Design, Fabrication, and Testing of a Constant-Force Microinjector . . . . .</b>	91
5.1 Introduction . . . . .	91
5.2 Structure Design . . . . .	92
5.2.1 Design of Displacement Amplifier . . . . .	92
5.2.2 Design of Zero-Stiffness Mechanism . . . . .	94
5.2.3 Parametric Study . . . . .	96
5.2.4 Design of Parameters and Optimization . . . . .	99
5.2.5 Design of the Layout . . . . .	101
5.3 Performance Evaluation with FEA Simulation . . . . .	102
5.3.1 Amplification Ratio Assessment . . . . .	102
5.3.2 Actuation Force and Stress Evaluation . . . . .	103
5.4 Performance Testing by Experimental Study . . . . .	105
5.4.1 Prototype Fabrication . . . . .	105
5.4.2 Testing Result of Constant-Force Performance . . . . .	106
5.4.3 Repeatability Testing Result . . . . .	107
5.4.4 Comparison Experimental Result . . . . .	109
5.5 Applications in Biological Micromanipulation . . . . .	110
5.5.1 Experimental Setup . . . . .	110
5.5.2 Controller Design . . . . .	111
5.5.3 Mechanical Property Testing of Biological Cell . . . . .	112
5.5.4 Experimental Testing of Cell Injection . . . . .	114
5.6 Conclusion . . . . .	116
References . . . . .	116
<b>6 Design, Modeling, and Control of a Constant-Force Microgripper . . . . .</b>	119
6.1 Introduction . . . . .	119
6.2 Mechanism Design . . . . .	121
6.2.1 Design of the System Stiffness . . . . .	121
6.2.2 Design of the Constant-Force Module . . . . .	122
6.3 Simulation Study with FEA . . . . .	125
6.4 Design of Sliding Mode Control . . . . .	129
6.4.1 Nonswitching-Type Reaching Law Design . . . . .	129
6.4.2 Stability Analysis . . . . .	131
6.5 Prototype Fabrication and Performance Testing . . . . .	132
6.5.1 Prototype Fabrication . . . . .	132
6.5.2 Gripping Range and Hysteresis Tests . . . . .	133
6.5.3 Force–Displacement Relation Test . . . . .	135
6.5.4 Dynamics Performance Test . . . . .	135
6.6 Closed-Loop Experimental Studies . . . . .	137
6.6.1 Resolution Testing Result . . . . .	138
6.6.2 Grasp-Hold-Release Operation Testing Result . . . . .	139

6.6.3	Further Discussion . . . . .	141
6.7	Conclusion . . . . .	142
	References . . . . .	142
<b>7</b>	<b>Design and Development of a Flexure-Based Compact Constant-Force Robotic Gripper . . . . .</b>	<b>145</b>
7.1	Introduction . . . . .	145
7.2	Mechanism Design . . . . .	147
7.2.1	Design of Constant-Force Module . . . . .	147
7.2.2	Design of Gripper Jaw Module . . . . .	148
7.2.3	Design of the Gripper Layout . . . . .	149
7.3	Parametric Design . . . . .	152
7.3.1	Actuation Force Consideration . . . . .	153
7.3.2	Gripping Force and Gripping Stroke Consideration . . . . .	153
7.3.3	Parametric Study . . . . .	158
7.4	Experimental Investigations . . . . .	160
7.4.1	Prototype Development . . . . .	160
7.4.2	Performance Testing Results . . . . .	161
7.4.3	Biological Gripping Application . . . . .	163
7.4.4	Comparison Study Result . . . . .	164
7.4.5	Further Discussion . . . . .	165
7.5	Conclusion . . . . .	166
	References . . . . .	166
<b>8</b>	<b>Design and Implementation of a Force-Sensing MEMS Microgripper . . . . .</b>	<b>169</b>
8.1	Introduction . . . . .	169
8.2	Mechanism Design of the Microgripper . . . . .	170
8.2.1	Actuator Design . . . . .	172
8.2.2	Sensor Design . . . . .	174
8.3	Performance Estimation with FEA Simulation . . . . .	177
8.3.1	Statics Analysis . . . . .	178
8.3.2	Cross-Axis Sensitivity Analysis . . . . .	179
8.3.3	Dynamics Analysis . . . . .	180
8.4	Prototype Fabrication . . . . .	182
8.5	Calibration and Performance Testing . . . . .	182
8.5.1	Force Sensor Calibration . . . . .	182
8.5.2	Gripping Range Testing . . . . .	185
8.5.3	Bio-Cellulose Grasp Operation . . . . .	187
8.5.4	Further Discussion . . . . .	188
8.6	Conclusions . . . . .	189
	References . . . . .	189

<b>9 Design, Analysis, and Development of a Piezoelectric Microsyringe Pump . . . . .</b>	191
9.1 Introduction . . . . .	191
9.2 Mechanism Design . . . . .	192
9.2.1 Design of Displacement Amplifier . . . . .	192
9.2.2 Design of Parallelogram Flexure . . . . .	194
9.3 Optimization Design and Simulation Study . . . . .	195
9.3.1 Optimization Setup . . . . .	195
9.3.2 Optimization Results . . . . .	195
9.3.3 Simulation Results . . . . .	196
9.4 Prototype Development and Experimental Results . . . . .	199
9.4.1 Prototype Fabrication and Assembly . . . . .	199
9.4.2 Controller Setup . . . . .	201
9.4.3 Microsyringe Performance Testing Results . . . . .	202
9.4.4 Microsyringe Pump Performance Testing Results . . . . .	204
9.5 Conclusion . . . . .	207
References . . . . .	207
<b>10 Visual Servo Control with Force Regulation for Microinjection . . . . .</b>	209
10.1 Introduction . . . . .	209
10.2 Experimental Setup . . . . .	210
10.3 Image Processing Procedure . . . . .	212
10.3.1 Detection of the Injector . . . . .	213
10.3.2 Detection of the Cells . . . . .	215
10.4 Control Scheme Design . . . . .	216
10.4.1 Cell Searching Process . . . . .	217
10.4.2 Cell Piercing Process . . . . .	218
10.5 Experimental Results . . . . .	220
10.6 Conclusion . . . . .	221
References . . . . .	222
<b>Index . . . . .</b>	225

be operated manually by two hands of human operator under a microscope. While one hand immobilizes the cell using a glass pipette with suction force, the other hand penetrates the cell embryo with a sharp pipette and then injects exogenous materials into the cell. However, manual injection suffers from low efficiency, low success rate, and low repeatability. Moreover, the long-time operation will cause fatigue to the human operator.

Alternatively, robotic micro-manipulation system allows the realization of precision positioning, gripping, and velocity control of micro-objects by integrating actuation, sensing, and control of the micro-robotic system. Such technology enables the dynamic exploration of objects in micro/nanoworld, and scale new height for the development on new material, information technology, manufacturing equipment,