

WIRELESSLY ACTIVATED THERMO-RESPONSIVE POLYMERS
FOR IMPLANTABLE DRUG DELIVERY AND CENTRIFUGAL
MICROFLUIDIC DEVICE APPLICATIONS

MOHAMMAD AMRI BIN ZAINAL

A thesis submitted in fulfilment of the
requirements for the award of the degree of
Doctor of Philosophy (Electrical Engineering)

School of Electrical Engineering
Faculty of Engineering
Universiti Teknologi Malaysia

DECEMBER 2021

DEDICATION

I dedicate this thesis to my beloved family. Mak, Abah, sibling, my beloved wife, and children whose prayer, patience, support, and love have made toward the end of this journey.

ACKNOWLEDGEMENT

Alhamdulillah, praised be to Allah, Who has granted me the strength and courage to complete this thesis. The peace and blessing of Allah are due to His Messenger, the prophet Muhammad.

First of all, I would like to express my deepest gratitude to my supervisor, Assoc. Prof. Ir. Dr. Mohamed Sultan Mohamed Ali, for giving me the opportunity to work in his research. His continuous guidance, advice, and support throughout my studies have made the completion of this research.

Special acknowledgment to the Ministry of Science, Technology, and Innovation, Malaysia (MOSTI), Ministry of Higher Education, Malaysia (MOHE), and Universiti Teknologi Malaysia (UTM) for their financial support during my research years.

Finally, I wish to express honest gratitude to my parents and family. The support and encouragement are appreciated, especially to my wife, Rosnani Abdullah, and my children, Anna Najla and Amirul Naim. Without their sacrifice, I would have never been able to accomplish this far.

ABSTRACT

Thermo-responsive polymers have a great potential to be used in various types of microdevices. Besides being low cost, lightweight, and easy to process, the material properties can be easily tuned by altering the polymer chemistry and structure. These preferences have resulted in their application in many fields, including those in biomedical. Nevertheless, their advantages have not been fully exploited. For instance, most of the actuation mechanisms typically by increasing materials temperature using Joule heating which requires wired interfaces, thus restricting their applications where access and space are crucial. This thesis reports a novel technique for the wireless control of thermo-responsive polymers microactuators and microvalve. The wireless control of thermo-responsive polymers utilizes a radiofrequency magnetic field wireless heating of planar inductor-capacitor circuit to directly heat the actuator/valve, without the use of additional circuits is demonstrated. To function as a cantilever type microactuator, a shape-memory polymer bonded directly with a heater is fabricated. The actuation range of 140 μm as the tip opening distance is achieved at device temperature 44 $^{\circ}\text{C}$ in 30 s using 0.05 W radio frequency (RF) power. An application of a drug delivery device integrated with the proposed actuator is demonstrated. The actuator is successfully operated in water through wireless activation diffusing acidic solution with an average release rate of 0.172 $\mu\text{L}/\text{min}$. Wireless actuated microvalve using paraffin wax for the centrifugal microfluidic compact disc is also presented and evaluated. Experimental characterization shows a valve operated within ~ 100 s of activation using RF power of 1 W that provides a temperature increase up to 42 $^{\circ}\text{C}$ at a disc rotation speed of 200 rpm. The presented RF wireless control scheme of thermo-responsive polymer would provide an opportunity to extend further their potential of application beyond this report.

ABSTRAK

Polimer tindakbalas haba mempunyai potensi yang banyak untuk digunakan didalam pelbagai jenis alatan mikro. Selain murah, ringan, dan mudah diproses, sifat bahan juga dapat disesuaikan dengan mengubah struktur atau komposisi kimia polimer. Kelebihan ini membolehkan ianya diaplikasikan didalam pelbagai bidang asuk bidang bioperubatan. Walaupun begitu, ia masih belum dimanfaatkan sepenuhnya. Sebagai contoh, mekanisme pengaktifan biasanya dilakukan dengan meningkatkan suhu bahan menerusi pemanasan Joule yang mana ia memerlukan antaramuka berwayar. Teknik ini membataskan potensi aplikasi didalam situasi dimana akses dan ruang menjadi keutamaan. Tesis ini melaporkan teknik baru bagi kawalan tanpa wayar penggerak-mikro polimer dan injap-mikro, menggunakan polimer tindakbalas haba. Kawalan tanpa wayar polimer ini diaplikasi menggunakan medan magnet frekuensi radio menerusi pemanasan tanpa wayar litar leper induktor-kapasitor, bagi memanaskan penggerak / injap secara langsung, tanpa penggunaan litar tambahan. Polimer bentuk memori yang diintegrasikan dengan pemanas juga telah dibangunkan yang berfungsi sebagai penggerak-mikro jenis kantilever. Jarak pembukaan $140\ \mu\text{m}$ dicapai pada suhu peranti $44\ ^\circ\text{C}$ dalam masa 30 s menggunakan kuasa radio frekuensi (RF) 0.05 W. Aplikasi alatan penyampaian ubat yang diintegrasikan dengan penggerak juga dibentangkan. Penggerak berjaya dikendalikan di dalam air melalui pengaktifan tanpa wayar di dalam larutan berasid, dengan purata kadar pelepasan cecair $0.172\ \mu\text{L}/\text{min}$. Selain daripada itu, injap mikro yang digerakkan tanpa wayar menggunakan lilin parafin bagi applikasi cakera padat emparan mikrocecair, juga dibentangkan dan dinilai. Pencirian melalui eksperimen menunjukkan injap dapat dikendalikan dalam masa $\sim 100\ \text{s}$ selepas pengaktifan dengan menggunakan kuasa RF 1 W, dimana ianya berjaya menaikkan suhu sehingga $42\ ^\circ\text{C}$ pada kelajuan putaran cakera 200 rpm. Skim kawalan tanpa wayar RF polimer tindakbalas haba yang dibentangkan ini berpotensi untuk diperluaskan lagi aplikasinya di luar laporan ini.

TABLE OF CONTENTS

	TITLE	PAGE
	DECLARATION	ii
	DEDICATION	iii
	ACKNOWLEDGEMENT	iv
	ABSTRACT	v
	ABSTRAK	vi
	TABLE OF CONTENTS	vii
	LIST OF TABLES	x
	LIST OF FIGURES	xi
	LIST OF ABBREVIATIONS	xiv
	LIST OF SYMBOLS	xvi
CHAPTER 1	INTRODUCTION	1
1.1	Introduction	1
1.2	Problem Statement	3
1.3	Research Objective	4
1.4	Scope of Research	4
1.5	Research Contribution	5
1.6	Potential Impact of Research	6
1.7	Thesis Outline	7
CHAPTER 2	LITERATURE REVIEW	9
2.1	Introduction	9
2.2	Thermo-Responsive Materials	9
2.2.1	Shape Memory Alloys	10
2.2.2	Shape Memory Polymers	11
2.2.2.1	Classification of SMPs	12
2.2.2.2	Properties	14
2.2.2.3	Actuation Principle & Design	16

2.2.3	Paraffin Wax	19
2.2.3.1	Properties of Paraffin Wax	20
2.2.3.2	Actuation Principle and Design	23
2.2.4	Selection of Thermo Responsive Material	24
2.3	Implantable Drug Delivery Device Systems	24
2.3.1	Classification ofl DDS	25
2.3.2	Passive IDDS	26
2.3.3	Active IDDS	28
2.3.4	MEMS IDDS	31
2.3.4.1	MEMS actuator	32
2.3.4.2	Wirelessly Activated IDDS	35
2.4	Microfluidics and Lab-on-a-Disc	38
2.4.1	Pumping	39
2.4.2	Valving	40
2.4.2.1	Non-Mechanical Microvalve	43
2.4.3	Microfluidic Classification	46
2.4.4	Lab-on-a-Disc	48
2.5	Chapter Summary	51
CHAPTER 3	METHODOLOGY	53
3.1	Introduction	53
3.2	Research Methodology	53
3.3	General Experimental Setup and Apparatus	56
3.4	Chapter Summary	57
CHAPTER 4	FREQUENCY-CONTROLLED SHAPE MEMORY POLYMER MICROACTUATOR FOR DRUG DELIVERY APPLICATION	59
4.1	Introduction	59
4.2	Design and simulation of the drug reservoir and SMP microactuator	59
4.2.1	Drug reservoir	61
4.2.2	Microheater	62

4.2.3	SMP microactuator	65
4.2.4	Simulation result	66
4.2.4.1	SMP thickness effects toward displacement	68
4.2.4.2	Curing temperature effect towards displacement	69
4.3	Device fabrication	70
4.4	Experimental result and discussion	73
4.4.1	SMP characterization	73
4.4.2	Thermal response of the actuator	74
4.4.3	Wireless release demonstration	81
4.5	Chapter Summary	84
CHAPTER 5	WIRELESS VALVING FOR CENTRIFUGAL MICROFLUIDIC DISC	85
5.1	Introduction	85
5.2	Design and Working Principle	85
5.3	Device Fabrication	88
5.4	Experimental Results and Discussion	90
5.4.1	Resonant Frequency Measurement	90
5.4.2	Heat Distribution on the Disc	91
5.4.3	Wireless VCV Test	95
5.4.4	Mixing Demonstration	96
5.4.5	Performance Comparison	98
5.5	Chapter Summary	98
CHAPTER 6	CONCLUSION AND FUTURE WORK	101
6.1	Conclusion	101
6.2	Future works	103
	REFERENCES	105
	LIST OF PUBLICATIONS	141

LIST OF TABLES

TABLE NO.	TITLE	PAGE
Table 2.1	Properties comparison between SMPs and SMAs [46]	15
Table 2.2	Thermophysical properties of paraffin wax [86].	23
Table 2.3	Various MEMS actuation types, working principles, and properties. Table 2.3	33
Table 4.1	Different values of N and their respected d_{out} , d_{avg} , ρ , and f_c .	65
Table 4.2	Microactuator design range.	67
Table 4.3	The mechanical and thermomechanical properties of SMP, PI, and Cu.	67
Table 5.1	Performance comparison of paraffin wax-based active valving techniques.	99

LIST OF FIGURES

FIGURE NO.	TITLE	PAGE
Figure 2.1	General classification of SMPs based on their shape memory function, chemical structure, and activation methods.	13
Figure 2.2	Illustration of the mechanism for one-way SME.	17
Figure 2.3	Energy densities of common actuation materials for microactuators [78].	20
Figure 2.4	Melting point (°C) as a function of chain length for linear alkanes, [78], [79].	21
Figure 2.5	Specific volume for <i>n</i> -tetracosane (C ₂₄ H ₅₀) as a function for temperature for pressure between 0 to 200 Mpa[78], [82].	22
Figure 2.6	General classification of IDDS	25
Figure 2.7	The type (non-biodegradable and biodegradable) reservoir and matrix IDDS.	27
Figure 2.8	Pharmacokinetic profiles as a function of time for conventional and controlled release deliveries [133].	29
Figure 2.9	Common unit operations for a microfluidic system.	39
Figure 2.10	Microfluidic pumping classification based on mechanical and non-mechanical types. Figure 2.10	41
Figure 2.11	The general classification of microvalves.	42
Figure 2.12	Range of (a) Pressure (kPa), and (b) time response (s) for different actuators used in microvalves, [213].	45
Figure 2.13	Range of (a) Power (W), and Voltage (V), for different actuators used in microvalves [317].	46
Figure 2.14	Microfluidic platform classification based on liquid propulsion principle.	47
Figure 2.15	A basic microfluidic disc with source and destination chamber. The annotations represent the parameter used to calculate the centrifugal pressure.	49
Figure 3.1	General overview of methodology steps followed in this thesis	54
Figure 3.2	General experimental setup for both devices.	57

Figure 4.1	(a) Device conceptual diagram and working principle of frequency sensitive wireless heater, (b) bottom-side isometric view of SMP microactuator with wireless heater, and the device body.	60
Figure 4.2	The design and dimension of the reservoir (in <i>mm</i>) (a) isometric view, (b) top view, (c) Front view.	62
Figure 4.3	Circular shape planar inductor realization based on Current Sheet Approximation, [340].	64
Figure 4.4	Final design of planar inductor and top capacitor plate, (a) top view, (b) isometric view.	65
Figure 4.5	The design and dimension of SMP polymer (in <i>mm</i>) (a) top view, (b) isometric view.	66
Figure 4.6	The result from finite element analysis when the curing temperature is 90 °C with 50 μm of SMP thickness.	68
Figure 4.7	Microactuator SMP thickness vs. displacement.	69
Figure 4.8	Curing temperature vs. displacement of SMP.	70
Figure 4.9	Heater fabrication process (a-e), (a) bottom-side: etch Cu, (b) bottom-side: Cu electroplating, (c) view after completing bottom side, (d) top-side: etch Cu, (e) top-side: bond SMP with bottom-side of completed heaters, (f) device body with PDMS on cavity, (g) illustration of a complete device, (h) fabricated device.	72
Figure 4.10	(a) DSC curve of SMP, (b) reflective coefficient, S_{11} measurement of the heater measured on-air and in DI water using a network analyzer.	74
Figure 4.11	Experimental setup for the wireless test.	75
Figure 4.12	(a) Thermal response of the heater when subjected RF power of 0.05 W in DI water, (b) thermal image showing the heat distribution of the actuator after 30 s activation with 0.05 W of RF power on-air, (c) temporal changes in the temperature when the heater is wirelessly resonated with different RF output power of 0.05 W, 0.10 W, and 0.15 W respectively on air.	76
Figure 4.13	(a) Actuator displacement and temperature vs. time with the response to 30 s on / 1 min off activation, (b) actuator displacement and temperature vs. time with the response to 10 s on / 1 min off activation.	79
Figure 4.14	Repeatability test subjected to 500 times actuation cycle. The RF power output is 0.05 W with a 10s / 30s on/off period.	80

Figure 4.15	Captured images for ending interval of on-off cycles, (a) set1:30s/3min on-off cycles, (b) set2:10s /2min on-off cycles, (c) color concentration vs. time (min).	82
Figure 4.16	pH changes (measured) and released amounts of pH buffer (calculated) vs. actuator activated time.	83
Figure 5.1	The working principle and designs, (a) conceptual diagram of the device, (b) selective control of frequency sensitive wireless heater,(c) microfluidics and chambers design on a disc with the respective location of vacuum/compression valve and mixing application.	87
Figure 5.2	3D model illustration for construction of the microfluidic disc.	88
Figure 5.3	(a) Step of heater fabrication using a photolithography process, (b) topside view of a completed heater.	89
Figure 5.4	S11 measurement of the transmitter antenna, Heater 1, and Heater 2.	91
Figure 5.5	Experimental setup, (a) illustration, (b) actual setup.	92
Figure 5.6	Thermal image around the heater area captured when the device was stationary.	92
Figure 5.7	(a) Disc thermal image captured during rotation, (b) thermal images nearby the heater's area measured at different rotation speeds, (c) graph of temperature vs. speed and the trendline.	94
Figure 5.8	Wireless demonstration of RF controlled active valve on microfluidic disc; (a) vacuum valve, (b) compression valve.	96
Figure 5.9	(a) Selective RF controlled of vacuum valve for mixing application, (b) graph of volume in destination chamber vs. time for the mixing application.	97

LIST OF ABBREVIATIONS

AC	-	Alternating current
BTB	-	Bromothymol Blue
cm ²	-	Squaredcentimeter
CTE	-	Coefficient of thermal expansion
Cu	-	Copper / Cuprum
Cu-clad	-	Copper-clad
Cu ₂ SO ₄	-	Copper Sulfate
DCM	-	Dichloromethane
DI	-	Deionized
DSC	-	Differential scanning calorimetry
DSLR		Digital single-lens reflex
HCl	-	Hydrochloric Acid
Hz	-	Hertz
IR	-	Infrared
LC	-	Inductor-capacitor
LOC	-	Lab-on-a-chip
mA	-	Miliampere
MEMS	-	Microelectromechanical Systems
MHz	-	Megahertz
min	-	Minute
°C	-	Degrees Celcius
PDMS	-	Polydimethylsiloxane
PI	-	Polyimide
PMMA	-	polymethyl methacrylate
PSA	-	Pressure-sensitive adhesive
RF	-	Radio frequency
s	-	Second
SMA	-	Shape Memory Alloy
SMM	-	Shape Memory Material
SMP	-	Shape Memory Polymer

TWSME - Two-way shape memory effect
VCV - Vacuum/compression valve
W - Watt

LIST OF SYMBOLS

f_c	-	Heater circuit resonant frequency
f_m	-	Electromagnetic field frequency
f_r	-	Resonant frequency
f_{r_air}	-	Resonant frequency on air
$f_{r_DI\ water}$	-	Resonant frequency on DI water
m_1	-	Slope line 1
m_2	-	Slope line 2
m_3	-	Slope line 3
S_{11}	-	S11 parameter
T_g	-	Glass transition temperature
T_{g_end}	-	Ending of the glass transition temperature
T_{g_start}	-	Starting of the glass transition temperature

CHAPTER 1

INTRODUCTION

1.1 Introduction

Microelectromechanical Systems (MEMS) are developed using a technology that combines the properties of electrical, mechanical, or other elements (i.e., magnetic, thermal, etc.), into a micro-scaled system. These systems are typically fabricated using conventional semiconductor batch processing techniques. They are miniature in size, ranging from millimeters down to nanometers. This technology has enabled various approaches in the biomedical field, such as pain management [1], cardiac pacemakers [2], minimally invasive robotic-assisted surgery [3], lab-on-a-chip (LOC) [4], and drug delivery [5].

Among these applications, LOC and drug delivery have received much attention from the scientific community due to their significant impact in medicine. The LOC platform is based on microfluidics, which is the study of micro-scaled fluid dynamics. LOC technology affects drug delivery advancements in various aspects, including drug carrier manufacturing, screening and their delivery.

With the accelerated development of new medicinal compounds, new drug delivery systems are needed to overcome the challenges associated with traditional drug delivery systems. One of the solutions is by introducing an implantable drug delivery system. MEMS are promising candidates for the development of novel implantable drug delivery systems that address existing problems. The system allows the delivery of various drugs with high therapeutic effectiveness by offering electromechanical control, multiple function integration, and miniaturization.

In recent decades, studies and application of MEMS in implantable drug delivery systems, especially on microactuators, have focused on their drug release mechanism. Microactuators are designed and developed using different methods that accommodate targeted applications. These devices are often operated using electrostatic, piezoelectric, electromagnetic and electrothermal principles, and may be made of shape-memory materials (SMMs).

In addition to drug delivery, the MEMS technology was used in microfluidic devices. This specific type of device comprises of microfluidic unit operations that allow for assay miniaturization, integration, automation, and parallelization of biochemical processes. The devices are typically classified by their type of liquid propulsion systems [6], such as capillary, acoustic, electrokinetic, pressure-driven, and centrifugal. A centrifugal-based microfluidic system is preferable as it does not require an external pumping mechanism to move the fluid inside the microfluidic channels. This would facilitate the integration of several microfluidic unit operations on a single platform.

The ability to operate MEMS devices wirelessly is also important to support the implantable nature and their portability. One approach to this wireless scheme is to utilize an active actuation mechanism, which is commonly defined by a battery-powered device. However, this approach tends to develop a bigger device with limited power longevity. The passive actuation mechanism, often known as batteryless actuation, is a better option for addressing these issues. Passive actuation uses acoustic waves, magnetic fields, ultrasonic, or inductive coupling mechanisms.

An inductive coupling mechanism is preferable to selectively control multiple devices. In this technique, a radio frequency (RF) magnetic field is used to transfer power from the transmitter to the receiver coil on the device. This transferred power is dissipated as heat, which is then used to control thermal-based actuators such as shape memory alloy (SMA), shape memory polymer (SMP), or paraffin wax.

Thermal-based SMA is advantageous due to its ability to provide high actuation stress. However, SMA is relatively expensive and requires a complex fabrication process to fabricate a device. A thermal-based polymer such as SMP or paraffin wax is preferable. Apart from being relatively cheaper and easier to process than SMA, the polymer has excellent mechanical properties, is flexible, and is biocompatible.

This thesis reports a novel wireless control of a thermo-responsive polymer-based microactuator and microvalve. The thermo-responsive polymers utilize RF magnetic field wireless heating of the planar inductor-capacitor circuit to directly heat the actuator or valve. Both devices are demonstrated in implantable drug delivery and microfluidic disc applications, respectively.

1.2 Problem Statement

Although there are numerous development of microactuators and microvalves, the ability to miniaturize and deploy these devices in implantable and portable applications is still limited. There are many obstacles and issues related to their powering, actuation, and integration. Thus far, such devices are commonly bound to the use of onboard batteries to activate the device. This method is not convenient for long-term implants and portable devices. Moreover, battery-powered devices require extra circuitry that increase their size. In contrast to the active type of actuators, passively operated actuators offer the ability to be scaled down in size. Scaling down reduces the cost of the system, while ensuring greater robustness and longevity. In addition, passively controlled systems are more appealing for implantable devices as they are safer for a longer period of use before replacement.

The passively controlled wireless actuation mechanism have been studied previously. However, their application in the wirelessly driven microactuator and microvalve have not been well explored, and their actuation mechanism requires further improvement, especially for the thermal-based type. There are reports on wireless activated thermal-based microactuators that used SMA [7], [8]. However, SMA is known to be expensive and requires complex processes and machines to process. The thermal-based wireless actuation mechanism still requires further research.

1.3 Research Objective

The main objectives of this research are to investigate 1) an implantable drug delivery device and 2) a centrifugal microfluidic device, activated by a thermo-responsive material that is powered and controlled wirelessly using an external magnetic field. The specific objectives are:

- i. To develop a
- ii. of the developed devices, including their temporal and thermal responses.

1.4 Scope of Research

The scope of this research focuses on the development of two wirelessly controlled devices for specific applications, namely, a microactuator for drug delivery applications and a microvalve system for centrifugal microfluidic disc application. The wireless actuation schemes are based on a thermal-responsive polymer. Furthermore, this scheme was employed in inductor-capacitor (LC) circuits designed for wireless activation of the devices.

For the fabrication process of the devices, the standard MEMS fabrication technique, including photolithography, etching, electroplating, and micromachining were used. The Cu-clad Polyimide (PI) was used to realize the LC circuit, while bulk polymethyl methacrylate (PMMA) was utilized to fabricate the drug reservoir and microfluidic centrifugal disc. The thermal-based SMP and paraffin wax was used to realize the microactuator and microvalve, respectively.

The Solidworks[®] software was used for the physical design. The thermal responses of the LC heaters and the thermomechanical behavior of the microactuators were simulated using (finite element analysis) FEA simulations by mean of COMSOL Multiphysics[®]. For characterization, thermal analysis was measured using an infrared (IR) thermal camera, displacement sensing was measured using a laser displacement sensor, S_{11} parameters were evaluated using a network analyzer and imagery data were obtained using microscopic imaging and digital single-lens reflex (DSLR) camera.

1.5 Research Contribution

This research proposes three significant contributions, with the utilization of the two different wirelessly controlled devices consisting of a thermo-responsive material as a medium of activation. These contributions are highlighted as follows:

- i. Development of a novel wireless LC planar microheater with minimal fabrication process, employing double-sided Cu-clad Polyimide (PI). This process eliminates the material deposition step and significantly reduces the time required to fabricate the heater.
- ii. Development of a novel implantable drug delivery device actuated by an SMP/PI laminate that exhibits two-way actuation. The device is operated using a passive frequency-sensitive wireless planar LC heater integrated with the SMP and enabled by an external magnetic field.

- iii. Development of novel selective wireless RF-controlled active valves for a microfluidic disc platform using field frequency modulation. The LC resonant circuit served as a frequency-sensitive wireless heater that provides localized heating with minimal power transmission.

1.6 Potential Impact of Research

Several factors are associated with the rather low application of MEMS-based actuators in biomedicine. One of these factors is the use of a conventional wired powering method, which limits mobility. To date, onboard batteries and biofuel cells are potential solutions to this issue. However, these approaches increase the size of the systems, subsequently limiting their operation and range of application. A passive RF wireless control system to drive the actuators, would allow further coping improvements and widen their number of possible applications.

One of the potential applications of the actuators is in implantable drug delivery devices. With this approach, the size and method of powering are important to provide minimum invasiveness and long-term operations. Furthermore, the ability to wirelessly control multiple actuators that are integrated into a single device in a selective manner will be advantageous in implantable and microfluidic devices. Integration of the actuator's component and the LC circuit can greatly reduce fabrication complexity, size, and cost of the device. Furthermore, the LC circuit fabricated using double-sided Cu-clad PI, was proven to require only a few steps, thus reducing the number of steps required [7], [8]. In addition, the use of polymers that are flexible and easier to process may initiate a rapid development of MEMS-based microactuators and microvalves. The positive outcomes from this research are expected to promote advances in the technology of devices used in biomedicine and beyond.

1.7 Thesis Outline

This thesis is divided into six chapters. Chapter 1 is a general overview of MEMS technology, implantable drug delivery, and microfluidic systems. This is followed by the problem statement, objectives, and scope of the research. Chapter 2 presents the literature review, which covers an overview of thermo-responsive materials, implantable drug delivery device systems, and microfluidic devices in greater depth. MEMS actuation mechanisms, material properties, and actuation methods are also covered in their respective applications. Chapter 3 presents the methodology, followed by Chapter 4, which covers the development of a frequency controlled SMP microactuator for implantable drug delivery devices. Chapter 5 presents a novel wireless valving for a centrifugal microfluidic disc and demonstrates its ability to selectively activate multiple actuators, as well as valve performance. Finally, the thesis concludes with Chapter 6, where the key results and directions for future work are discussed, followed by a list of publications resulting from this work.

REFERENCES

- [1] G. Sathiyabama, S. S. Krishnan, D. Saravanan, and R. S. Kumaran, "Bio-MEMS based sensor for acute and chronic pain management: An online measurement strategy for using biomedical MEMS sensor in the assessment of pain intensity and study of inflammation," in *Proceedings - NCET NRES EM 2014: 2nd IEEE National Conference on Emerging Trends in New and Renewable Energy Sources and Energy Management*, 2015, pp. 227–230.
- [2] O. L. Bockeria, M. B. Biniashvili, T. G. Le, A. S. Satyukova, D. K. Zhiengaliev, and V. A. Shvartz, "Mini-invasive technique of implanting the first domestic wireless epicardial pacemaker with a MEMS-converter," *Russian Open Medical Journal*, vol. 9, no. 2, 2020.
- [3] A. Nakai, K. Kuwana, K. Saito, T. Dohi, A. Kumagai, and I. Shimoyama, "MEMS 6-axis force-torque sensor attached to the tip of grasping forceps for identification of tumor in thoracoscopic surgery," in *Proceedings of the IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, 2017, pp. 546–548.
- [4] S. Chen and M. H. Shamsi, "Biosensors-on-chip: A topical review," *Journal of Micromechanics and Microengineering*, vol. 27, no. 8, 2017.
- [5] H. J. Lee, N. Choi, E.-S. Yoon, and I.-J. Cho, "MEMS devices for drug delivery," *Advanced Drug Delivery Reviews*, vol. 128, pp. 132–147, 2018.
- [6] D. Mark, S. Haeberle, G. Roth, F. Von Stetten, and R. Zengerle, "Microfluidic lab-on-a-chip platforms: Requirements, characteristics and applications," *Chem. Soc. Rev.*, vol. 39, no. 3, pp. 1153–1182, 2010.
- [7] M. S. Mohamed Ali and K. Takahata, "Wireless microfluidic control with integrated shape-memory-alloy actuators operated by field frequency modulation," *Journal of Micromechanics and Microengineering*, vol. 21, no. 7, 2011.
- [8] M. S. Mohamed Ali and K. Takahata, "Frequency-controlled wireless shape-memory-alloy microactuators integrated using an electroplating bonding process," *Sensors and Actuators A: Physical*, vol. 163, no. 1, pp. 363–372, Sep. 2010.

- [9] L. Sun, W. M. Huang, Z. Ding, Y. Zhao, C. C. Wang, H. Purnawali, and C. Tang, "Stimulus-responsive shape memory materials: A review," *Materials and Design*, vol. 33, no. 1, pp. 577–640, 2012.
- [10] W. M. Huang, Z. Ding, C. C. Wang, J. Wei, Y. Zhao, and H. Purnawali, "Shape memory materials," *Materials Today*, vol. 13, no. 7–8, pp. 54–61, 2010.
- [11] B. Andrawes and R. Desroches, "Unseating prevention for multiple frame bridges using superelastic devices," *Smart Materials and Structures*, vol. 14, no. 3, pp. S60–S67, 2005.
- [12] K. Otsuka and T. Kakeshita, "Science and technology of shape-memory alloys: New developments," *MRS Bulletin*, vol. 27, no. 2, pp. 91–98, 2002.
- [13] J. N. Kudva, "Overview of the DARPA smart wing project," *Journal of Intelligent Material Systems and Structures*, vol. 15, no. 4, pp. 261–267, 2004.
- [14] J. P. Dunne, D. M. Pitt, E. V. White, and E. Garcia, "Ground demonstration of the smart inlet," in *41st Structures, Structural Dynamics, and Materials Conference and Exhibit*, 2000.
- [15] L. Petrini and F. Migliavacca, "Biomedical applications of shape memory alloys," *J. Metall.*, vol. 2011, pp. 1–15, 2011.
- [16] E. J. Graesser and F. A. Cozzarelli, "Shape-memory alloys as new materials for aseismic isolation," *Journal of Engineering Mechanics*, vol. 117, no. 11, pp. 2590–2608, 1991.
- [17] W. Small IV, T. S. Wilson, P. R. Buckley, W. J. Benett, J. M. Loge, J. Hartman, and D. J. Maitland, "Prototype fabrication and preliminary In Vitro testing of a shape memory endovascular thrombectomy device," *IEEE Transactions on Biomedical Engineering*, vol. 54, no. 9, pp. 1657–1666, 2007.
- [18] Y. Haga, M. Mizushima, T. Matsunaga, and M. Esashi, "Medical and welfare applications of shape memory alloy microcoil actuators," *Smart Materials and Structures*, vol. 14, no. 5, pp. S266–S272, 2005.
- [19] S. Bossi, S. Micera, A. Menciassi, S. Kammer, T. D'Amico, and K. P. Hoffmann, "An Implantable Microactuated Intrafascicular Electrode for Peripheral Nerves," *IEEE Transactions on Biomedical Engineering*, vol. 56, no. 11, pp. 2701–2706, 2009.

- [20] S. Murad, J. Murad, and H. Khan, "A smarter sma technology for the realization of drug delivering endoscopic capsule," *Rawal Medical Journal*, vol. 38, no. 1, pp. 66–74, 2013.
- [21] S. Miyazaki, H. Y. Kim, and H. Hosoda, "Development and characterization of Ni-free Ti-base shape memory and superelastic alloys," *Materials Science and Engineering A*, vol. 438–440, no. SPEC. ISS., pp. 18–24, 2006.
- [22] R. E. McMahon, J. Ma, S. V. Verkhoturov, D. Munoz-Pinto, I. Karaman, F. Rubitschek, H. J. Maier, and M. S. Hahn, "A comparative study of the cytotoxicity and corrosion resistance of nickel-titanium and titanium-niobium shape memory alloys," *Acta Biomaterialia*, vol. 8, no. 7, pp. 2863–2870, 2012.
- [23] M. U. Farooq, F. A. Khalid, H. Zaigham, and I. H. Abidi, "Superelastic behaviour of Ti-Nb-Al ternary shape memory alloys for biomedical applications," *Materials Letters*, vol. 121, pp. 58–61, 2014.
- [24] M. Lai, Y. Gao, B. Yuan, and M. Zhu, "Effect of Pore Structure Regulation on the Properties of Porous TiNbZr Shape Memory Alloys for Biomedical Application," *Journal of Materials Engineering and Performance*, vol. 24, no. 1, pp. 136–142, 2015.
- [25] M. F. Ijaz, H. Y. Kim, H. Hosoda, and S. Miyazaki, "Superelastic properties of biomedical (Ti-Zr)-Mo-Sn alloys," *Materials Science and Engineering C*, vol. 48, pp. 11–20, 2015.
- [26] P. Surbled, C. Clerc, B. Le Pioufle, M. Ataka, and H. Fujita, "Effect of the composition and thermal annealing on the transformation temperatures of sputtered TiNi shape memory alloy thin films," *Thin Solid Films*, vol. 401, no. 1–2, pp. 52–59, 2001.
- [27] N. Sandström, S. Braun, G. Stemme, and W. Van Der Wijngaart, "Full wafer integration of shape memory alloy microactuators using adhesive bonding," in *TRANSDUCERS 2009 - 15th International Conference on Solid-State Sensors, Actuators and Microsystems*, 2009, pp. 845–848.
- [28] C. A. Biffi, A. Nespoli, B. Previtali, E. Villa, and A. Tuissi, "Functional response of NiTi elements for smart micro-actuation applications," *Journal of Materials Engineering and Performance*, vol. 23, no. 7, pp. 2351–2356, 2014.

- [29] J. Wang and J. Wang, "Shape memory effect of TiNi-based springs trained by constraint annealing," *Metals and Materials International*, vol. 19, no. 2, pp. 295–301, 2013.
- [30] J. Karger-Kocsis and S. Káráki, "Review of progress in shape memory epoxies and their composites," *Polymers*, vol. 10, no. 1, 2017.
- [31] J. Leng, H. Lu, Y. Liu, W. M. Huang, and S. Du, "Shape-memory polymers - A class of novel smart materials," *MRS Bulletin*, vol. 34, no. 11, pp. 848–855, 2009.
- [32] F. Xie, L. Huang, J. Leng, and Y. Liu, "Thermoset shape memory polymers and their composites," *Journal of Intelligent Material Systems and Structures*, vol. 27, no. 18, pp. 2433–2455, 2016.
- [33] Y. Wu, J. Hu, C. Zhang, J. Han, Y. Wang, and B. Kumar, "A facile approach to fabricate a UV/heat dual-responsive triple shape memory polymer," *Journal of Materials Chemistry A*, vol. 3, no. 1, pp. 97–100, 2015.
- [34] J. R. Kumpfer and S. J. Rowan, "Thermo-, photo-, and chemo-responsive shape-memory properties from photo-cross-linked metallo-supramolecular polymers," *Journal of the American Chemical Society*, vol. 133, no. 32, pp. 12866–12874, 2011.
- [35] F. Memarian, A. Fereidoon, and M. Ghorbanzadeh Ahangari, "The shape memory, and the mechanical and thermal properties of TPU/ABS/CNT: A ternary polymer composite," *RSC Advances*, vol. 6, no. 103, pp. 101038–101047, 2016.
- [36] G. S. Martins, I. M. Pereira, and R. L. Orfice, "Toughening brittle polymers with shape memory polymers," *Polymer*, vol. 135, pp. 30–38, 2018.
- [37] F. Khademeh Molavi, I. Ghasemi, M. Messori, and M. Esfandeh, "Nanocomposites based on poly(L-lactide)/poly(ϵ -caprolactone) blends with triple-shape memory behavior: Effect of the incorporation of graphene nanoplatelets (GNPs)," *Composites Science and Technology*, vol. 151, pp. 219–227, 2017.
- [38] L. Peponi, V. Sessini, M. P. Arrieta, I. Navarro-Baena, A. Sonseca, F. Dominici, E. Gimenez, L. Torre, A. Tercjak, D. López, and J. M. Kenny, "Thermally-activated shape memory effect on biodegradable nanocomposites based on PLA/PCL blend reinforced with hydroxyapatite," *Polymer Degradation and Stability*, vol. 151, pp. 36–51, 2018.

- [39] W. M. Huang, B. Yang, L. An, C. Li, and Y. S. Chan, "Water-driven programmable polyurethane shape memory polymer: Demonstration and mechanism," *Applied Physics Letters*, vol. 86, no. 11, pp. 1–3, 2005.
- [40] Y. Zhao, C. C. Wang, W. M. Huang, and H. Purnawali, "Ethanol induced shape recovery and swelling in poly(methyl methacrylate) and applications in fabrication of microlens array," *Adv Sci Technol*, vol. 77, pp. 354–358, 2013.
- [41] Q. Song, H. Chen, S. Zhou, K. Zhao, B. Wang, and P. Hu, "Thermo- and pH-sensitive shape memory polyurethane containing carboxyl groups," *Polymer Chemistry*, vol. 7, no. 9, pp. 1739–1746, 2016.
- [42] M. Zelzer and R. V. Ulijn, *Enzyme-responsive polymers: Properties, synthesis and applications*. 2014, pp. 166–203.
- [43] J. Cui and A. Del Campo, *Photo-responsive polymers: Properties, synthesis and applications*. 2014, pp. 93–133.
- [44] C. M. Jackson, R. Wagner, and R. Wasilewski, "55-Nitinol - The Alloy with a Memory: It's Physical Metallurgy Properties, and Applications. NASA SP-5110," 1972.
- [45] T. Xie, "Recent advances in polymer shape memory," *Polymer*, vol. 52, no. 22, pp. 4985–5000, 2011.
- [46] S. K. Melly, L. Liu, Y. Liu, and J. Leng, "Active composites based on shape memory polymers: overview, fabrication methods, applications, and future prospects," *Journal of Materials Science*, vol. 55, no. 25, pp. 10975–11051, 2020.
- [47] P. T. Mather, X. Luo, and I. A. Rousseau, "Shape memory polymer research," *Annual Review of Materials Research*, vol. 39, pp. 445–471, 2009.
- [48] B. Dietsch and T. Tong, "A review - Features and benefits of shape memory polymers (SMPs)," *Journal of Advanced Materials*, vol. 39, no. 2, pp. 3–12, 2007.
- [49] M. Behl, J. Zotzmann, and A. Lendlein, "Shape-memory polymers and shape-changing polymers," *Advances in Polymer Science*, vol. 226, no. 1, pp. 1–40, 2010.
- [50] C. M. Yakacki and K. Gall, "Shape-memory polymers for biomedical applications," *Advances in Polymer Science*, vol. 226, no. 1, pp. 147–175, 2010.

- [51] J. Delaey, P. Dubruel, and S. Van Vlierberghe, “Shape-Memory Polymers for Biomedical Applications,” *Advanced Functional Materials*, vol. 30, no. 44, 2020.
- [52] E. Yarali, A. Taheri, and M. Baghani, “A comprehensive review on thermomechanical constitutive models for shape memory polymers,” *Journal of Intelligent Material Systems and Structures*, vol. 31, no. 10, pp. 1243–1283, 2020.
- [53] Y. Xia, Y. He, F. Zhang, Y. Liu, and J. Leng, “A Review of Shape Memory Polymers and Composites: Mechanisms, Materials, and Applications,” *Advanced Materials*, 2020.
- [54] A. Boudjellal, D. Trache, K. Khimeche, S. L. Hafsaoui, A. Bougamra, A. Tcharkhtchi, and J.-F. Durastanti, “Stimulation and reinforcement of shape-memory polymers and their composites: A review,” *Journal of Thermoplastic Composite Materials*, 2020.
- [55] P. Mora, H. Schäfer, C. Jubsilp, S. Rimdusit, and K. Koschek, “Thermosetting Shape Memory Polymers and Composites Based on Polybenzoxazine Blends, Alloys and Copolymers,” *Chemistry - An Asian Journal*, vol. 14, no. 23, pp. 4129–4139, 2019.
- [56] M. Zare, M. P. Prabhakaran, N. Parvin, and S. Ramakrishna, “Thermally-induced two-way shape memory polymers: Mechanisms, structures, and applications,” *Chemical Engineering Journal*, vol. 374, pp. 706–720, 2019.
- [57] F. Li, Y. Liu, and J. Leng, “Progress of shape memory polymers and their composites in aerospace applications,” *Smart Materials and Structures*, vol. 28, no. 10, 2019.
- [58] W. Zhao, L. Liu, F. Zhang, J. Leng, and Y. Liu, “Shape memory polymers and their composites in biomedical applications,” *Materials Science and Engineering C*, vol. 97, pp. 864–883, 2019.
- [59] G. I. Peterson, A. V. Dobrynin, and M. L. Becker, “Biodegradable Shape Memory Polymers in Medicine,” *Advanced Healthcare Materials*, vol. 6, no. 21, 2017.
- [60] X.-L. Shen, G.-M. Zhu, and P.-F. Yang, “Biomedical Shape Memory Polymers,” *Cailiao Gongcheng/Journal of Materials Engineering*, vol. 45, no. 7, pp. 111–117, 2017.

- [61] C. Liu, H. Qin, and P. T. Mather, "Review of progress in shape-memory polymers," *Journal of Materials Chemistry*, vol. 17, no. 16, pp. 1543–1558, 2007.
- [62] K. Gall, P. Kreiner, D. Turner, and M. Hulse, "Shape-memory polymers for microelectromechanical systems," *Journal of Microelectromechanical Systems*, vol. 13, no. 3, pp. 472–483, 2004.
- [63] L. Sun, X. Gao, D. Wu, and Q. Guo, "Advances in Physiologically Relevant Actuation of Shape Memory Polymers for Biomedical Applications," *Polymer Reviews*, 2020.
- [64] C. M. Yakacki, R. Shandas, D. Safranski, A. M. Ortega, K. Sassaman, and K. Gall, "Strong, tailored, biocompatible shape-memory polymer networks," *Advanced Functional Materials*, vol. 18, no. 16, pp. 2428–2435, 2008.
- [65] R. Sujithra, S. M. Srinivasan, and A. Arockiarajan, "Shape recovery studies for coupled deformations in an epoxy based amorphous shape memory polymers," *Polymer Testing*, vol. 48, pp. 1–6, 2015.
- [66] K. Takashima, K. Sugitani, N. Morimoto, S. Sakaguchi, T. Noritsugu, and T. Mukai, "Pneumatic artificial rubber muscle using shape-memory polymer sheet with embedded electrical heating wire," *Smart Materials and Structures*, vol. 23, no. 12, 2014.
- [67] K. Hearon, L. D. Nash, B. L. Volk, T. Ware, J. P. Lewicki, W. E. Voit, T. S. Wilson, and D. J. Maitland, "Electron beam crosslinked polyurethane shape memory polymers with tunable mechanical properties," *Macromolecular Chemistry and Physics*, vol. 214, no. 11, pp. 1258–1272, 2013.
- [68] X. Luo and P. T. Mather, "Preparation and characterization of shape memory elastomeric composites," *Macromolecules*, vol. 42, no. 19, pp. 7251–7253, 2009.
- [69] X. Luo and P. T. Mather, "Design strategies for shape memory polymers," *Current Opinion in Chemical Engineering*, vol. 2, no. 1, pp. 103–111, 2013.
- [70] B. L. Volk, D. C. Lagoudas, and D. J. Maitland, "Characterizing and modeling the free recovery and constrained recovery behavior of a polyurethane shape memory polymer," *Smart Materials and Structures*, vol. 20, no. 9, 2011.

- [71] G. Li, G. Fei, B. Liu, H. Xia, and Y. Zhao, "Shape recovery characteristics for shape memory polymers subjected to high intensity focused ultrasound," *RSC Advances*, vol. 4, no. 62, pp. 32701–32709, 2014.
- [72] G. Li, G. Fei, H. Xia, J. Han, and Y. Zhao, "Spatial and temporal control of shape memory polymers and simultaneous drug release using high intensity focused ultrasound," *Journal of Materials Chemistry*, vol. 22, no. 16, pp. 7692–7696, 2012.
- [73] Y. Alapan, O. Yasa, O. Schauer, J. Giltinan, A. F. Tabak, V. Sourjik, and M. Sitti, "Soft erythrocyte-based bacterial microswimmers for cargo delivery," *Science Robotics*, vol. 3, no. 17, 2018.
- [74] M. Hu, H.-J. Butt, K. Landfester, M. B. Bannwarth, S. Wooh, and H. Thérien-Aubin, "Shaping the Assembly of Superparamagnetic Nanoparticles," *ACS Nano*, vol. 13, no. 3, pp. 3015–3022, 2019.
- [75] M. Li, Y. Wang, A. Chen, A. Naidu, B. S. Napier, W. Li, C. L. Rodriguez, S. A. Crooker, and F. G. Omenetto, "Flexible magnetic composites for light-controlled actuation and interfaces," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 115, no. 32, pp. 8119–8124, 2018.
- [76] W. Hu, G. Z. Lum, M. Mastrangeli, and M. Sitti, "Small-scale soft-bodied robot with multimodal locomotion," *Nature*, vol. 554, no. 7690, pp. 81–85, 2018.
- [77] P. Krulevitch, A. P. Lee, P. B. Ramsey, J. C. Trevino, J. Hamilton, and M. A. Northrup, "Thin film shape memory alloy microactuators," *Journal of Microelectromechanical Systems*, vol. 5, no. 4, pp. 270–282, 1996.
- [78] S. Ogden, L. Klintberg, G. Thornell, K. Hjort, and R. Bodén, "Review on miniaturized paraffin phase change actuators, valves, and pumps," *Microfluidics and Nanofluidics*, vol. 17, no. 1, pp. 53–71, 2014.
- [79] M. Freund, R. Csikós, S. Keszthelyi, and G. Y. Mózes, "Paraffin Products Properties, Technologies, Applications," *Paraffin Products: Properties, Technologies, Applications*, 1982.
- [80] H. Mehling and L. F. Cabeza, *Heat and Cold Storage with PCM*, 2008.
- [81] J. N. Lee, C. Park, and G. M. Whitesides, "Solvent Compatibility of Poly(dimethylsiloxane)-Based Microfluidic Devices," *Analytical Chemistry*, vol. 75, no. 23, pp. 6544–6554, 2003.

- [82] P. Zoller and D. J. Walsh, *Standard Pressure-Volume-Temperature Data for Polymers*, 1995.
- [83] J. Wang, S. J. Severtson, and A. Stein, “Significant and concurrent enhancement of stiffness, strength, and toughness for paraffin wax through organoclay addition,” *Advanced Materials*, vol. 18, no. 12, pp. 1585–1588, 2006.
- [84] J. Wang, S. J. Severtson, and P. H. Geil, “Brittle-ductile transitions and the toughening mechanism in paraffin/organo-clay nanocomposites,” *Materials Science and Engineering A*, vol. 467, no. 1–2, pp. 172–180, 2007.
- [85] A. Malik, S. Ogden, G. Amberg, and K. Hjort, “Modeling and analysis of a phase change material thermohydraulic membrane microactuator,” *Journal of Microelectromechanical Systems*, vol. 22, no. 1, pp. 186–194, 2013.
- [86] N. Ukrainczyk, S. Kurajica, and J. Å ipuÅ jiÅ Ą, “Thermophysical comparison of five commercial paraffin waxes as latent heat storage materials,” *Chemical and Biochemical Engineering Quarterly*, vol. 24, no. 2, pp. 129–137, 2010.
- [87] M. Lehto, J.-Å. Schweitz, and G. Thornell, “Binary mixtures of n-alkanes for tunable thermohydraulic microactuators,” *Journal of Microelectromechanical Systems*, vol. 16, no. 3, pp. 728–733, 2007.
- [88] J.-M. Park, Y.-K. Cho, B.-S. Lee, J.-G. Lee, and C. Ko, “Multifunctional microvalves control by optical illumination on nanoheaters and its application in centrifugal microfluidic devices,” *Lab Chip*, vol. 7, no. 5, pp. 557–564, 2007.
- [89] K. W. Oh, K. Namkoong, and C. Park, “A phase change microvalve using a meltable magnetic material: Ferro-Wax,” in *Micro Total Analysis Systems - Proceedings of MicroTAS 2005 Conference: 9th International Conference on Miniaturized Systems for Chemistry and Life Sciences*, 2005, vol. 1, pp. 554–556.
- [90] H. J. Sant, T. Ho, and B. K. Gale, “An in situ heater for a phase-change-material-based actuation system,” *Journal of Micromechanics and Microengineering*, vol. 20, no. 8, 2010.
- [91] L. Klintberg and G. Thornell, “A thermal microactuator made by partial impregnation of polyimide with paraffin,” *Journal of Micromechanics and Microengineering*, vol. 12, no. 6, pp. 849–854, 2002.

- [92] P. Dubois, E. Vela, S. Koster, D. Briand, H. R. Shea, and N.-F. De Rooij, "Paraffin-PDMS composite thermo microactuator with large vertical displacement capability," *Proc. 10th Int. Conf. New Actuators*, pp. 215–218, 2006.
- [93] W. Al-Faqheri, F. Ibrahim, T. H. G. Thio, J. Moebius, K. Joseph, H. Arof, and M. Madou, "Vacuum/Compression Valving (VCV) Using Paraffin-Wax on a Centrifugal Microfluidic CD Platform," *Plos One*, vol. 8, no. 3, 2013.
- [94] R. H. Liu, J. Bonanno, J. Yang, R. Lenigk, and P. Grodzinski, "Single-use, thermally actuated paraffin valves for microfluidic applications," *Sens. Actuators, B*, vol. 98, no. 2–3, pp. 328–336, 2004.
- [95] B. . Yang and Q. . Lin, "A latchable phase-change microvalve with integrated heaters," *J Microelectromech S*, vol. 18, no. 4, pp. 860–867, 2009.
- [96] J. Jonsson, S. Ogden, L. Johansson, K. Hjort, and G. Thornell, "Acoustically enriching, large-depth aquatic sampler," *Lab on a Chip*, vol. 12, no. 9, pp. 1619–1628, 2012.
- [97] J.-Y. Choi, J. Ruan, F. Coccetti, and S. Lucyszyn, "Three-dimensional RF MEMS switch for power applications," *IEEE Transactions on Industrial Electronics*, vol. 56, no. 4, pp. 1031–1039, 2009.
- [98] N. Rajgor, M. Patel, and V. H. Bhaskar, "Implantable drug delivery systems: An overview," *Systematic Reviews in Pharmacy*, vol. 2, no. 2, pp. 91–95, 2011.
- [99] V. Prasad Shastri, "Non-degradable biocompatible polymers in medicine: Past, present and future," *Current Pharmaceutical Biotechnology*, vol. 4, no. 5, pp. 331–337, 2003.
- [100] G. Zur, E. Linder-Ganz, J. J. Elsner, J. Shani, O. Brenner, G. Agar, E. B. Hershman, S. P. Arnoczky, F. Guilak, and A. Shterling, "Chondroprotective effects of a polycarbonate-urethane meniscal implant: Histopathological results in a sheep model," *Knee Surgery, Sports Traumatology, Arthroscopy*, vol. 19, no. 2, pp. 255–263, 2011.
- [101] J. Nunes-Pereira, S. Ribeiro, C. Ribeiro, C. J. Gombek, F. M. Gama, A. C. Gomes, D. A. Patterson, and S. Lanceros-MÃ©ndez, "Poly(vinylidene fluoride) and copolymers as porous membranes for tissue engineering applications," *Polymer Testing*, vol. 44, pp. 234–241, 2015.

- [102] M. J. L. Colaris, M. de Boer, R. R. van der Hulst, and J. W. Cohen Tervaert, “Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature,” *Immunologic Research*, vol. 65, no. 1, pp. 120–128, 2017.
- [103] F. MartÃ-nez-Rus, A. Ferreira, M. Ã-zcan, J. F. BartolomÃ©, and G. PradÃ-es, “Fracture resistance of crowns cemented on titanium and zirconia implant abutments: A comparison of monolithic versus manually veneered all-ceramic systems,” *International Journal of Oral and Maxillofacial Implants*, vol. 27, no. 6, pp. 1448–1455, 2012.
- [104] A. Kumar and J. Pillai, “Chapter 13 - Implantable drug delivery systems: An overview,” in *Nanostructures for the Engineering of Cells, Tissues and Organs*, A. M. Grumezescu, Ed. William Andrew Publishing, 2018, pp. 473–511.
- [105] L. W. Kleiner, J. C. Wright, and Y. Wang, “Evolution of implantable and insertable drug delivery systems,” *Journal of Controlled Release*, vol. 181, no. 1, pp. 1–10, 2014.
- [106] L. Mascarenhas, A. Van Beek, H. Coelingh Bennink, and J. Newton, “Twenty-four month comparison of apolipoproteins A-I, A-II, and B in contraceptive implant users (Norplant® and Implanon®) in Birmingham, United Kingdom,” *Contraception*, vol. 58, no. 4, pp. 215–219, 1998.
- [107] E. D. B. Johansson, “The return of the pharmaceutical industry to the market of contraception,” *Steroids*, vol. 65, no. 10–11, pp. 709–711, 2000.
- [108] A. Glasier, “Implantable contraceptives for women: Effectiveness, discontinuation rates, return of fertility, and outcome of pregnancies,” *Contraception*, vol. 65, no. 1, pp. 29–37, 2002.
- [109] I. Sivin, “Risks and benefits, advantages and disadvantages of levonorgestrel-releasing contraceptive implants,” *Drug Safety*, vol. 26, no. 5, pp. 303–335, 2003.
- [110] M. Oliveira-Ribeiro, C. A. Petta, L. A. L. De Angelo Andrade, M. M. Hidalgo, A. Pellogia, and L. Bahamondes, “Endometrial histology, microvascular density and caliber, and matrix metalloproteinase-3 in users of the Nestorone®-releasing contraceptive implant with and without endometrial breakthrough bleeding,” *Contraception*, vol. 73, no. 6, pp. 634–640, 2006.

- [111] D. R. Friend, “Advances in vaginal drug delivery,” *Drug Delivery and Translational Research*, vol. 1, no. 3, pp. 183–184, 2011.
- [112] K. H. Rademacher, H. L. Vahdat, L. Dorflinger, D. H. Owen, and M. J. Steiner, “Global introduction of a low-cost contraceptive implant,” *Critical Issues in Reproductive Health*, vol. 33, pp. 285–306, 2014.
- [113] V. Brache, “WHO Symposium WHO. Background and study methodology of a multicentre randomized clinical trial of two implantable contraceptives for women: Jadelle and Implanon,” *Eur. J. Contracept. Reproduct. Health Care*, vol. 19, p. 1, 2014.
- [114] S. Uhm, R. Pope, A. Schmidt, C. Bazella, and L. Perriera, “Home or office etonogestrel implant insertion after pregnancy: a randomized trial,” *Contraception*, vol. 94, no. 5, pp. 567–571, 2016.
- [115] J. C. Nickel, P. Jain, N. Shore, J. Anderson, D. Giesing, H. Lee, G. Kim, K. Daniel, S. White, C. Larrivee-Elkins, J. Lekstrom-Himes, and M. Cima, “Continuous intravesical lidocaine treatment for interstitial cystitis/bladder pain syndrome: Safety and efficacy of a new drug delivery device,” *Science Translational Medicine*, vol. 4, no. 143, 2012.
- [116] M. Iitzoe and M. Guarnieri, “New developments in managing opioid addiction: Impact of a subdermal buprenorphine implant,” *Drug Design, Development and Therapy*, vol. 11, pp. 1429–1437, 2017.
- [117] S. H. Lee and Y. B. Choy, “Implantable devices for sustained, intravesical drug delivery,” *International Neurourology Journal*, vol. 20, no. 2, pp. 101–106, 2016.
- [118] S. A. Grossman and N. Roberts, “Analgesic applications for a subcutaneous implant that continuously releases hydromorphone,” *European Journal of Pain Supplements*, vol. 5, no. 2, pp. 439–442, 2011.
- [119] E. Z. Herring, L. A. Frizon, O. Hogue, J. U. Mejia, R. Rosenquist, R. B. Bolash, A. G. Machado, and S. J. Nagel, “Long-term outcomes using intrathecal drug delivery systems in complex regional pain syndrome,” *Pain Medicine (United States)*, vol. 20, no. 3, pp. 515–520, 2019.
- [120] N. Sanchis-López, C. Romero-García, J. De Andres-Ibanez, R. Martínez-Plumed, P. Rodríguez-Gimillo, M. J. Hernández-Cáiz, and V. A.-L. de Medrano, “Medical device related pressure injury in the treatment

- of chronic pain: An early sign of explantation in suspected infection,” *Pain Physician*, vol. 21, no. 3, pp. E235–E246, 2018.
- [121] A. P. Tiwari, D. P. Bhattarai, B. Maharjan, S. W. Ko, H. Y. Kim, C. H. Park, and C. S. Kim, “Polydopamine-based Implantable Multifunctional Nanocarpet for Highly Efficient Photothermal-chemo Therapy,” *Scientific Reports*, vol. 9, no. 1, 2019.
- [122] H. Luo, Y. Zhang, Z. Yang, G. Zuo, Q. Zhang, F. Yao, and Y. Wan, “Encapsulating doxorubicin-intercalated lamellar nanohydroxyapatite into PLGA nanofibers for sustained drug release,” *Current Applied Physics*, vol. 19, no. 11, pp. 1204–1210, 2019.
- [123] M. Sedighi, F. Rahimi, A. H. Rezayan, M.-A. Shahbazi, D. Witzigmann, and J. Huwyler, “Combined cerium oxide nanocapping and layer-by-layer coating of porous silicon containers for controlled drug release,” *Journal of Materials Science*, vol. 53, no. 21, pp. 14975–14988, 2018.
- [124] M. J. Rowland, C. C. Parkins, J. H. McAbee, A. K. Kolb, R. Hein, X. J. Loh, C. Watts, and O. A. Scherman, “An adherent tissue-inspired hydrogel delivery vehicle utilised in primary human glioma models,” *Biomaterials*, vol. 179, pp. 199–208, 2018.
- [125] J. L. Bourges, C. Bloquel, A. Thomas, F. Froussart, A. Bochet, F. Azan, R. Gurny, D. BenEzra, and F. Behar-Cohen, “Intraocular implants for extended drug delivery: Therapeutic applications,” *Advanced Drug Delivery Reviews*, vol. 58, no. 11, pp. 1182–1202, 2006.
- [126] S. S. Lee, P. Yuan, and M. R. Robinson, “Ocular implants for drug delivery,” *Encyclopedia of Biomaterials and Biomedical Engineering*, pp. 2259–2269, 2008.
- [127] A. Than, C. Liu, H. Chang, P. K. Duong, C. M. G. Cheung, C. Xu, X. Wang, and P. Chen, “Self-implantable double-layered micro-drug-reservoirs for efficient and controlled ocular drug delivery,” *Nature Communications*, vol. 9, no. 1, 2018.
- [128] C. Wang, S.-J. Seo, J.-S. Kim, S.-H. Lee, J.-K. Jeon, J.-W. Kim, K.-H. Kim, J.-K. Kim, and J. Park, “Intravitreal implantable magnetic micropump for on-demand VEGFR-targeted drug delivery,” *Journal of Controlled Release*, vol. 283, pp. 105–112, 2018.

- [129] W.-W. Yang and E. Pierstorff, "Reservoir-based polymer drug delivery systems," *Journal of Laboratory Automation*, vol. 17, no. 1, pp. 50–58, 2012.
- [130] F. P. Pons-Faudoa, A. Ballerini, J. Sakamoto, and A. Grattoni, "Advanced implantable drug delivery technologies: transforming the clinical landscape of therapeutics for chronic diseases," *Biomedical Microdevices*, vol. 21, no. 2, 2019.
- [131] W. Tian, M. Mahmoudi, T. Lhermusier, S. Kiramijyan, F. Chen, R. Torguson, W. O. Suddath, L. F. Satler, A. D. Pichard, and R. Waksman, "The influence of advancing age on implantation of drug-eluting stents," *Catheterization and Cardiovascular Interventions*, vol. 88, no. 4, pp. 516–521, 2016.
- [132] J. Urquhart, J. W. Fara, and K. L. Willis, "Rate-controlled delivery systems in drug and hormone research," *Annual Review of Pharmacology and Toxicology*, vol. VOL. 24, pp. 199–236, 1984.
- [133] N. M. Elman and U. M. Upadhyay, "Medical applications of implantable drug delivery microdevices based on mems (micro-electro-mechanical-systems)," *Current Pharmaceutical Biotechnology*, vol. 11, no. 4, pp. 398–403, 2010.
- [134] R. A. Keraliya, C. Patel, P. Patel, V. Keraliya, T. G. Soni, R. C. Patel, and M. M. Patel, "Osmotic Drug Delivery System as a Part of Modified Release Dosage Form," *ISRN Pharmaceutics*, 2012.
- [135] K. D. Ethans, O. I. Schryvers, P. W. Nance, and A. R. Casey, "Intrathecal drug therapy using the Codman Model 3000 constant flow implantable infusion pumps: Experience with 17 cases," *Spinal Cord*, vol. 43, no. 4, pp. 214–218, 2005.
- [136] S. M. Rosen, T. A. Bromberg, G. Padda, J. Barsa, E. Dunbar, G. Dwarakanath, Y. Navalgund, T. Jaffe, T. L. Yearwood, M. Creamer, and T. Deer, "Intrathecal administration of infumorph[®] vs compounded morphine for treatment of intractable pain using the prometra[®] programmable pump," *Pain Medicine (United States)*, vol. 14, no. 6, pp. 865–873, 2013.
- [137] J. S. Speed and K. A. Hyndman, "In vivo organ specific drug delivery with implantable peristaltic pumps," *Scientific Reports*, vol. 6, 2016.
- [138] "Intrathecal Baclofen Therapy Systems - SynchroMed II," *Medtronic.com*, no. 22222, 2020.

- [139] R. C. Bourge, A. B. Waxman, M. Gomberg-Maitland, S. M. Shapiro, J. H. Tarver, D. L. Zwicke, J. P. Feldman, M. M. Chakinala, R. P. Frantz, F. Torres, J. Cerkvėnik, M. Morris, M. Thalin, L. Peterson, and L. J. Rubin, “Treprostinil Administered to Treat Pulmonary Arterial Hypertension Using a Fully Implantable Programmable Intravascular Delivery System: Results of the DelIVery for PAH Trial,” *Chest*, vol. 150, no. 1, pp. 27–34, 2016.
- [140] R. Bolash, B. Udeh, Y. Saweris, M. Guirguis, J. E. Dalton, N. Makarova, and N. Mekhail, “Longevity and cost of implantable intrathecal drug delivery systems for chronic pain management: A retrospective analysis of 365 patients,” *Neuromodulation*, vol. 18, no. 2, pp. 150–155, 2015.
- [141] R. Farra, N. F. Sheppard Jr., L. McCabe, R. M. Neer, J. M. Anderson, J. T. Santini Jr., M. J. Cima, and R. Langer, “First-in-human testing of a wirelessly controlled drug delivery microchip,” *Science Translational Medicine*, vol. 4, no. 122, 2012.
- [142] J. M. Maloney, S. A. Umland, B. F. Polito, N. F. Sheppard Jr., C. M. Pelta, and J. T. Santini Jr., “Electrothermally activated microchips for implantable drug delivery and biosensing,” *Journal of Controlled Release*, vol. 109, no. 1–3, pp. 244–255, 2005.
- [143] J.-C. Guti rrez-Hern ndez, S. Caffey, W. Abdallah, P. Calvillo, R. Gonz lez, J. Shih, J. Brennan, J. Zimmerman, J.-C. Mart nez-Camarillo, A. R. Rodr guez, R. Varma, A. Santos, G. S nchez, and M. Humayun, “One-Year Feasibility Study of Replenish MicroPump for Intravitreal Drug Delivery: A Pilot Study,” *Translational Vision Science & Technology*, vol. 3, no. 4, pp. 1–1, 2014.
- [144] E. Thielicke and E. Obermeier, “Microactuators and their technologies,” *Mechatronics*, vol. 10, no. 4, pp. 431–455, 2000.
- [145] W.-C. Chuang, H.-L. Lee, P.-Z. Chang, and Y.-C. Hu, “Review on the modeling of electrostatic MEMS,” *Sensors*, vol. 10, no. 6, pp. 6149–6171, 2010.
- [146] C. Huang, C. Christophorou, K. Najafi, A. Naguib, and H. M. Nagib, “An electrostatic microactuator system for application in high-speed jets,” *Journal of Microelectromechanical Systems*, vol. 11, no. 3, pp. 222–235, 2002.

- [147] F. Ceysens, S. Sadeghpour, H. Fujita, and R. Puers, “Actuators: Accomplishments, opportunities and challenges,” *Sensors and Actuators, A: Physical*, vol. 295, pp. 604–611, 2019.
- [148] S. Fatikow and U. Rembold, “Microactuators: Principles and Examples,” in *Microsystem Technology and Microrobotics*, Berlin, Heidelberg: Springer Berlin Heidelberg, 1997, pp. 109–208.
- [149] P. S. Sumant, A. C. Cangellaris, and N. R. Alum, “Modeling of dielectric charging in RF MEMS capacitive switches,” *Microwave and Optical Technology Letters*, vol. 49, no. 12, pp. 3188–3192, 2007.
- [150] C. Goldsmith, J. Ehmke, A. Malczewski, B. Pillans, S. Eshelman, Z. Yao, J. Brank, and M. Eberly, “Lifetime characterization of capacitive RF MEMS switches,” in *IEEE MTT-S International Microwave Symposium Digest*, 2001, vol. 3, pp. 227–230.
- [151] R. K. Jain, S. Majumder, and B. Ghosh, “Design and analysis of piezoelectric actuator for micro gripper,” *International Journal of Mechanics and Materials in Design*, vol. 11, no. 3, pp. 253–276, 2015.
- [152] Z. Ding, J. Dong, H. Yin, Z. Wang, X. Zhou, and Z. Xu, “Design and experimental performances of a piezoelectric stick-slip actuator for rotary motion,” in *IOP Conference Series: Materials Science and Engineering*, 2019, vol. 563, no. 4.
- [153] L. Wang, W. Chen, J. Liu, J. Deng, and Y. Liu, “A review of recent studies on non-resonant piezoelectric actuators,” *Mechanical Systems and Signal Processing*, vol. 133, 2019.
- [154] H. Shi, J. Chen, G. Liu, W. Xiao, and S. Dong, “A piezoelectric pseudo-bimorph actuator,” *Applied Physics Letters*, vol. 102, no. 24, 2013.
- [155] J. E. Huber, N. A. Fleck, and M. F. Ashby, “The selection of mechanical actuators based on performance indices,” *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences*, vol. 453, no. 1965, pp. 2185–2205, 1997.
- [156] N. J. Conway, Z. J. Traina, and S.-G. Kim, “A strain amplifying piezoelectric MEMS actuator,” *Journal of Micromechanics and Microengineering*, vol. 17, no. 4, pp. 781–787, 2007.
- [157] H. K. R. Kommepalli, H. G. Yu, C. L. Muhlstein, S. Trolrier-McKinstry, C. D. Rahn, and S. A. Tadigadapa, “Design, fabrication, and performance of a

- piezoelectric uniflex microactuator,” *Journal of Microelectromechanical Systems*, vol. 18, no. 3, pp. 616–625, 2009.
- [158] Y. Jing and J. Luo, “Structure and electrical properties of PMN-PZT micro-actuator deposited by tape-casting process,” *Journal of Materials Science: Materials in Electronics*, vol. 16, no. 5, pp. 287–294, 2005.
- [159] M. U. Khan, C. Prella, F. Lamarque, and S. Bättgenbach, “Design and Assessment of a Micropositioning System Driven by Electromagnetic Actuators,” *IEEE/ASME Transactions on Mechatronics*, vol. 22, no. 1, pp. 551–560, 2017.
- [160] C.-H. Ou, Y.-C. Lin, Y. Keikoin, T. Ono, M. Esashi, and Y.-C. Tsai, “Two-dimensional MEMS Fe-based metallic glass micromirror driven by an electromagnetic actuator,” *Japanese Journal of Applied Physics*, vol. 58, no. SD, 2019.
- [161] V. F.-G. Tseng, J. Li, X. Zhang, J. Ding, Q. Chen, and H. Xie, “An electromagnetically actuated micromirror with precise angle control for harsh environment optical switching applications,” *Sensors and Actuators, A: Physical*, vol. 206, pp. 1–9, 2014.
- [162] A. Potekhina and C. Wang, “Review of electrothermal actuators and applications,” *Actuators*, vol. 8, no. 4, 2019.
- [163] P. Jetty, S. Jayaram, J. Veinot, and M. Pratt, “Superficial femoral artery nitinol stent in a patient with nickel allergy,” *Journal of Vascular Surgery*, vol. 58, no. 5, pp. 1388–1390, 2013.
- [164] T. Maruyama and H. Kubo, *Ferrous (Fe-based) shape memory alloys (SMAs): Properties, processing and applications*. 2011, pp. 141–159.
- [165] M. H. and L. G., “A review of stimuli-responsive shape memory polymer composites,” *Polymer (United Kingdom)*, vol. 54, no. 9, pp. 2199–2221, 2013.
- [166] K. Wang, S. Strandman, and X. X. Zhu, “A mini review: Shape memory polymers for biomedical applications,” *Frontiers of Chemical Science and Engineering*, vol. 11, no. 2, pp. 1–11, 2017.
- [167] J. H. Prescott, S. Lipka, S. Baldwin, N. F. Sheppard Jr., J. M. Maloney, J. Coppeta, B. Yomtov, M. A. Staples, and J. T. Santini Jr., “Chronic, programmed polypeptide delivery from an implanted, multireservoir microchip device,” *Nature Biotechnology*, vol. 24, no. 4, pp. 437–438, 2006.

- [168] S. Smith, T. B. Tang, J. G. Terry, J. T. M. Stevenson, B. W. Flynn, H. M. Reekie, A. F. Murray, A. M. Gundlach, D. Renshaw, B. Dhillon, A. Ohtori, Y. Inoue, and A. J. Walton, "Development of a miniaturised drug delivery system with wireless power transfer and communication," *IET Nanobiotechnology*, vol. 1, no. 5, pp. 80–86, 2007.
- [169] T. B. Tang, S. Smith, B. W. Flynn, J. T. M. Stevenson, A. M. Gundlach, H. M. Reekie, A. F. Murray, D. Renshaw, B. Dhillon, A. Ohtori, Y. Inoue, J. G. Terry, and A. J. Walton, "Implementation of wireless power transfer and communications for an implantable ocular drug delivery system," *IET Nanobiotechnology*, vol. 2, no. 3, pp. 72–79, 2008.
- [170] K. Vollmers, D. R. Frutiger, B. E. Kratochvil, and B. J. Nelson, "Wireless resonant magnetic microactuator for untethered mobile microrobots," *Applied Physics Letters*, vol. 92, no. 14, 2008.
- [171] P. Basset, A. Kaiser, P. Bigotte, D. Collard, and L. Buchaillot, "A large stepwise motion electrostatic actuator for a wireless microrobot," in *Micro Electro Mechanical Systems, 2002. The Fifteenth IEEE International Conference on*, 2002, pp. 606–609.
- [172] L. H. Han and S. Chen, "Wireless bimorph micro-actuators by pulsed laser heating," *Sensors and Actuators, A: Physical*, vol. 121, no. 1, pp. 35–43, 2005.
- [173] S. S. Zaidi, F. Lamarque, J. Favergeon, O. Carton, C. Prella, M. Lejeune, and A. Zeinert, "Wavelength dependent remote power supply for shape memory alloy," *Journal of Intelligent Material Systems and Structures*, vol. 21, no. 2, pp. 175–184, 2010.
- [174] J. Fong, Z. Xiao, and K. Takahata, "Wireless implantable chip with integrated nitinol-based pump for radio-controlled local drug delivery," *Lab on a Chip - Miniaturisation for Chemistry and Biology*, vol. 15, no. 4, pp. 1050–1058, 2015.
- [175] S. K. Ahn, P. Deshmukh, and R. M. Kasi, "Shape memory behavior of side-chain liquid crystalline polymer networks triggered by dual transition temperatures," *Macromolecules*, vol. 43, no. 17, pp. 7330–7340, 2010.
- [176] J. Li, W. R. Rodgers, and T. Xie, "Semi-crystalline two-way shape memory elastomer," *Polymer*, vol. 52, no. 23, pp. 5320–5325, 2011.

- [177] S. Chen, J. Hu, H. Zhuo, and Y. Zhu, "Two-way shape memory effect in polymer laminates," *Materials Letters*, vol. 62, no. 25, pp. 4088–4090, 2008.
- [178] H. Tamagawa, "Thermo-responsive two-way shape changeable polymeric laminate," *Materials Letters*, vol. 64, no. 6, pp. 749–751, 2010.
- [179] H. Tamagawa, K. Kikuchi, and G. Nagai, "Mechanical characteristics of a thermo-responsive two-way shape change polymeric laminate," *Sensors and Actuators, A: Physical*, vol. 163, no. 1, pp. 356–362, 2010.
- [180] X. Q. . b Feng, G. Z. . Zhang, Q. M. . Bai, H. Y. . Jiang, B. . Xu, and H. J. . Li, "High Strength Self-Healing Magnetic Elastomers with Shape Memory Effect," *Macromolecular Materials and Engineering*, vol. 301, no. 2, pp. 125–132, 2016.
- [181] S. Y. Gu, S. P. Jin, X. F. Gao, and J. Mu, "Polylactide-based polyurethane shape memory nanocomposites (Fe₃O₄/PLAUs) with fast magnetic responsiveness," *Smart Materials and Structures*, vol. 25, no. 5, 2016.
- [182] T. Weigel, R. Mohr, and A. Lendlein, "Investigation of parameters to achieve temperatures required to initiate the shape-memory effect of magnetic nanocomposites by inductive heating," *Smart Mater. Struct.*, vol. 18, no. 2, 2009.
- [183] Y. Wang, R. Zhao, S. Wang, Z. Liu, and R. Tang, "In vivo dual-targeted chemotherapy of drug resistant cancer by rationally designed nanocarrier," *Biomaterials*, vol. 75, pp. 71–81, 2016.
- [184] D. J. Maitland, M. F. Metzger, D. Schumann, A. Lee, and T. S. Wilson, "Photothermal properties of shape memory polymer micro-actuators for treating stroke," *Lasers in Surgery and Medicine*, vol. 30, no. 1, pp. 1–11, 2002.
- [185] F. P. Du, E. Z. Ye, W. Yang, T. H. Shen, C. Y. Tang, X. L. Xie, X. P. Zhou, and W. C. Law, "Electroactive shape memory polymer based on optimized multi-walled carbon nanotubes/polyvinyl alcohol nanocomposites," *Composites Part B: Engineering*, vol. 68, pp. 170–175, 2015.
- [186] H. Lu, Y. Yao, and L. Lin, "Carbon-based reinforcement in shape-memory polymer composite for electrical actuation," *Pigment and Resin Technology*, vol. 43, no. 1, pp. 26–34, 2014.
- [187] G. M. Whitesides, "The origins and the future of microfluidics," *Nature*, vol. 442, no. 7101, pp. 368–373, 2006.

- [188] T. M. Squires and S. R. Quake, "Microfluidics: Fluid physics at the nanoliter scale," *Reviews of Modern Physics*, vol. 77, no. 3, pp. 977–1026, 2005.
- [189] S. Takayama, E. Ostuni, P. LeDuc, K. Naruse, D. E. Ingber, and G. M. Whitesides, "Subcellular positioning of small molecules," *Nature*, vol. 411, no. 6841, p. 1016, 2001.
- [190] J. Son, R. Samuel, B. K. Gale, D. T. Carrell, and J. M. Hotaling, "Separation of sperm cells from samples containing high concentrations of white blood cells using a spiral channel," *Biomicrofluidics*, vol. 11, no. 5, 2017.
- [191] A. Bange, H. B. Halsall, and W. R. Heineman, "Microfluidic immunosensor systems," *Biosensors and Bioelectronics*, vol. 20, no. 12, pp. 2488–2503, 2005.
- [192] C. L. Hansen, E. Skordalakest, J. M. Berger, and S. R. Quake, "A robust and scalable microfluidic metering method that allows protein crystal growth by free interface diffusion," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 99, no. 26, pp. 16531–16536, 2002.
- [193] A. R. Jafek, S. Harbertson, H. Brady, R. Samuel, and B. K. Gale, "Instrumentation for xPCR Incorporating qPCR and HRMA," *Analytical Chemistry*, vol. 90, no. 12, pp. 7190–7196, 2018.
- [194] A. Manz, D. J. Harrison, E. M. J. Verpoorte, J. C. Fettinger, A. Paulus, H. LÃ¼di, and H. M. Widmer, "Planar chips technology for miniaturization and integration of separation techniques into monitoring systems. Capillary electrophoresis on a chip," *Journal of Chromatography A*, vol. 593, no. 1–2, pp. 253–258, 1992.
- [195] C. D. Chin, V. Linder, and S. K. Sia, "Commercialization of microfluidic point-of-care diagnostic devices," *Lab on a Chip*, vol. 12, no. 12, pp. 2118–2134, 2012.
- [196] S. Mross, S. Pierrat, T. Zimmermann, and M. Kraft, "Microfluidic enzymatic biosensing systems: A review," *Biosensors and Bioelectronics*, vol. 70, pp. 376–391, 2015.
- [197] P. Gravesen, J. Branebjerg, and O. S. Jensen, "Microfluidics - A review," *Journal of Micromechanics and Microengineering*, vol. 3, no. 4, pp. 168–182, 1993.

- [198] C. Yi, C.-W. Li, S. Ji, and M. Yang, "Microfluidics technology for manipulation and analysis of biological cells," *Analytica Chimica Acta*, vol. 560, no. 1–2, pp. 1–23, 2006.
- [199] D. Belder, "Microfluidics with droplets," *Angewandte Chemie - International Edition*, vol. 44, no. 23, pp. 3521–3522, 2005.
- [200] H. G. Kerkhoff, "Testing microelectronic biofluidic systems," *IEEE Design and Test of Computers*, vol. 24, no. 1, pp. 72–82, 2007.
- [201] J. C. McDonald, D. C. Duffy, J. R. Anderson, D. T. Chiu, H. Wu, O. J. A. Schueller, and G. M. Whitesides, "Fabrication of microfluidic systems in poly(dimethylsiloxane)," *Electrophoresis*, vol. 21, no. 1, pp. 27–40, 2000.
- [202] T. L. Liu, X. Wen, Y.-C. Kung, and P.-Y. C. Cru, "Fabrication strategy for micro soft robotics with semiconductor devices integration," in *Proceedings of the IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, 2017, pp. 663–666.
- [203] F. Arai, K. Kotani, H. Maruyama, A. Honda, and M. Ejima, "On-chip robotics for biomedical innovation: Manipulation of single virus on a chip," in *2009 9th IEEE Conference on Nanotechnology, IEEE NANO 2009*, 2009, pp. 113–118.
- [204] R. W. Barber and D. R. Emerson, "Optimal design of microfluidic networks using biologically inspired principles," *Microfluidics and Nanofluidics*, vol. 4, no. 3, pp. 179–191, 2008.
- [205] A. J. Chung, B. Cordovez, N. Jasuja, D. J. Lee, X. T. Huang, and D. Erickson, "Implantable microfluidic and electronic systems for insect flight manipulation," *Microfluidics and Nanofluidics*, vol. 13, no. 2, pp. 345–352, 2012.
- [206] K. D. Jones, M. Nakashima, C. J. Bradshaw, J. Papadopoulos, and M. F. Platzer, "On flow separation control by means of flapping wings," *Bio-mechanisms of Swimming and Flying, Chap 5*, 2004.
- [207] P. N. Nge, C. I. Rogers, and A. T. Woolley, "Advances in microfluidic materials, functions, integration, and applications," *Chemical Reviews*, vol. 113, no. 4, pp. 2550–2583, 2013.
- [208] V. TesařTM, "Microfluidic Valves for Flow Control at Low Reynolds Numbers," *Journal of Visualization*, vol. 4, no. 1, pp. 51–60, 2001.

- [209] M. Safdar, J. JÃ¶niss, and S. SÃ¡nchez, "Microfluidic fuel cells for energy generation," *Lab on a Chip*, vol. 16, no. 15, pp. 2754–2758, 2016.
- [210] M. T. Guo, A. Rotem, J. A. Heyman, and D. A. Weitz, "Droplet microfluidics for high-throughput biological assays," *Lab on a Chip*, vol. 12, no. 12, pp. 2146–2155, 2012.
- [211] J.-Y. Qian, C.-W. Hou, X.-J. Li, and Z.-J. Jin, "Actuation mechanism of microvalves: A review," *Micromachines*, vol. 11, no. 2, 2020.
- [212] G. T. A. Kovacs, *Micromachined Transducers Sourcebook*, 1998.
- [213] N. T. Nguyen, S. T. Wereley, and S. A. M. Shaegh, "Microfluidics for Internal Flow Control: Microvalves," in *Fundamentals and Applications of Microfluidics, Third Edition*, Artech House, 2019, pp. 211–254.
- [214] O. Ducloux, Y. Deblock, A. Talbi, L. Gimeno, N. Tiercelin, P. Pernod, V. Preobrazhensky, and A. Merlen, "Magnetically actuated microvalves for active flow control," *Solid Mechanics and its Applications*, vol. 7, pp. 59–65, 2008.
- [215] P. J. Chang, F. W. Chang, M. C. Yuen, R. Otilar, and D. A. Horsley, "Force measurements of a magnetic micro actuator proposed for a microvalve array," *Journal of Micromechanics and Microengineering*, vol. 24, no. 3, 2014.
- [216] T. Suzuki, J. Suzuki, K. Terao, H. Takao, F. Shimokawa, F. Oohira, and H. Miyagawa, "Development of magnetically driven microvalve using photosensitive SU-8/Fe composite," *International Journal of Applied Electromagnetics and Mechanics*, vol. 52, no. 3–4, pp. 1585–1590, 2016.
- [217] A. Pradeep, S. V. Raj, J. Stanley, and T. G. S. Babu, "Design, Simulation and Fabrication of a Normally-Closed Microvalve based on Magnetic Actuation," in *Materials Today: Proceedings*, 2018, vol. 5, no. 8, pp. 16059–16064.
- [218] X. Liu and S. Li, "An Electromagnetic Microvalve for Pneumatic Control of Microfluidic Systems," *Journal of Laboratory Automation*, vol. 19, no. 5, pp. 444–453, 2014.
- [219] X. Liu and S. Li, "Control method experimental research of micro chamber air pressure via a novel electromagnetic microvalve," in *Proceedings - 2017 4th International Conference on Information Science and Control Engineering, ICISCE 2017*, 2017, pp. 921–925.

- [220] S. Messner, J. Schaible, H. Sandmaier, and R. Zengerle, “Three-way silicon microvalve for pneumatic applications with electrostatic actuation principle,” *Microfluidics and Nanofluidics*, vol. 2, no. 2, pp. 89–96, 2006.
- [221] B. Bae, J. Han, R. I. Masel, and M. A. Shannon, “A bidirectional electrostatic microvalve with microsecond switching performance,” *Journal of Microelectromechanical Systems*, vol. 16, no. 6, pp. 1461–1471, 2007.
- [222] S. Messner, J. Schaible, P. Nommensen, and R. Zengerle, “Electrostatically driven 3-way silicon microvalve for pneumatic applications,” *Sensors and Materials*, vol. 19, no. 1, pp. 57–78, 2007.
- [223] Q. Zhang, N. Pekas, and D. Juncker, “Design and fabrication of novel compliant electrostatically actuated microvalves,” *Advanced Materials Research*, vol. 74, pp. 179–182, 2009.
- [224] E. Yildirim, A. KoyuncuoÇşlu, and H. KÃ¼lah, “An electrostatic parylene microvalve for controlling in-plane flow,” in *Proceedings of Conference, MicroTAS 2009 - The 13th International Conference on Miniaturized Systems for Chemistry and Life Sciences*, 2009, pp. 1034–1036.
- [225] J. D. Tice, A. V. Desai, T. A. Bassett, G. A. Ten Eyck, C. A. Apblett, and P. J. A. Kenis, “Electrostatically actuated microvalves fabricated with soft lithographic techniques,” in *Proceedings of Conference, MicroTAS 2009 - The 13th International Conference on Miniaturized Systems for Chemistry and Life Sciences*, 2009, pp. 1674–1676.
- [226] E. Yildirim, A. KoyuncuoÇşlu, and H. KÃ¼lah, “An electrostatic parylene microvalve for lab-on-a-chip applications [Ã¶ip-Ã¼stÃ¼-laboratuvar uygulamalari iÃ¼sin elektrostatik mikro kapak tasarimi],” in *2010 15th National Biomedical Engineering Meeting, BIYOMUT2010*, 2010.
- [227] K. Yoshida, S. Tanaka, Y. Hagihara, S. Tomonari, and M. Esashi, “Normally closed electrostatic microvalve with pressure balance mechanism for portable fuel cell application,” *Sensors and Actuators, A: Physical*, vol. 157, no. 2, pp. 290–298, 2010.
- [228] K. Yoshida, S. Tanaka, Y. Hagihara, S. Tomonari, and M. Esashi, “Normally closed electrostatic microvalve with pressure balance mechanism for portable fuel cell application. Part I: Design and simulation,” *Sensors and Actuators, A: Physical*, vol. 157, no. 2, pp. 299–306, 2010.

- [229] J. D. Tice, A. V. Desai, T. A. Bassett, C. A. Apblett, and P. J. A. Kenis, “Electrostatic microvalves for integrated microchemical systems,” in *15th International Conference on Miniaturized Systems for Chemistry and Life Sciences 2011, MicroTAS 2011*, 2011, vol. 3, pp. 1813–1815.
- [230] E. Yildirim and H. K lah, “Analysis and characterization of an electrostatically actuated in-plane parylene microvalve,” *Journal of Micromechanics and Microengineering*, vol. 21, no. 10, 2011.
- [231] E. Yildirim, H. Kulah, and M. A. S. Arikan, “An electrostatically actuated parylene microvalve for lab-on-a-chip applications,” in *2011 16th International Solid-State Sensors, Actuators and Microsystems Conference, TRANSDUCERS’11*, 2011, pp. 250–253.
- [232] T. Dankovic and A. Feinerman, “Electrostatically actuated compliant microvalve,” in *ASME International Mechanical Engineering Congress and Exposition, Proceedings (IMECE)*, 2012, vol. 9, no. PARTS A AND B, pp. 721–729.
- [233] E. Yildirim, M. A. S. Arikan, and H. K lah, “A normally closed electrostatic parylene microvalve for micro total analysis systems,” *Sensors and Actuators, A: Physical*, vol. 181, pp. 81–86, 2012.
- [234] D. Anjewierden, G. A. Liddiard, and B. K. Gale, “An electrostatic microvalve for pneumatic control of microfluidic systems,” *Journal of Micromechanics and Microengineering*, vol. 22, no. 2, 2012.
- [235] E. Yildirim, E. Zg r, and H. K lah, “A droplet based multi-drug screening system controlled with electrostatic microvalves,” in *Proceedings of the 16th International Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2012*, 2012, pp. 959–961.
- [236] J. D. Tice, J. B. Rosheck, C. D. Hamlin, C. A. Apblett, and P. J. A. Kenis, “Normally-closed electrostatic microvalve fabricated using exclusively soft-lithographic techniques and operated with portable electronics,” *Journal of Microelectromechanical Systems*, vol. 22, no. 6, pp. 1251–1253, 2013.
- [237] M. Li and D. Li, “Microvalve using electrokinetic motion of electrically induced Janus droplet,” *Analytica Chimica Acta*, vol. 1021, pp. 85–94, 2018.
- [238] B. A. Bucci, J. S. Viperman, W. Clark, J. Peter Hensel, J. Thornton, and S. Kim, “Piezoelectric microvalve for flow control in polymer electrolyte fuel

- cells,” in *American Society of Mechanical Engineers, Advanced Energy Systems Division (Publication) AES*, 2006.
- [239] A. Doll, M. Wischke, H.-J. Schrag, A. Geipel, F. Goldschmidtboeing, and P. Woias, “Characterization of active silicon microvalves with piezoelectric membrane actuators,” *Microelectronic Engineering*, vol. 84, no. 5–8, pp. 1202–1206, 2007.
- [240] I. Fazal and M. C. Elwenspoek, “Design and analysis of a high pressure piezoelectric actuated microvalve,” *Journal of Micromechanics and Microengineering*, vol. 17, no. 11, pp. 2366–2379, 2007.
- [241] I. Fazal and M. C. Elwenspoek, “Piezoelectric microvalve for precise control of gas flow at high pressure,” in *2007 Proceedings of the ASME International Design Engineering Technical Conferences and Computers and Information in Engineering Conference, DETC2007*, 2008, vol. 3 PART B, pp. 841–844.
- [242] A. Gunda, G. Å-zkayar, M. Tichem, and M. K. Ghatkesar, “Proportional microvalve using a unimorph piezoelectric microactuator,” *Micromachines*, vol. 11, no. 2, 2020.
- [243] C. Lee, E.-H. Yang, S. M. Saeidi, and J. M. Khodadadi, “Fabrication, characterization, and computational modeling of a piezoelectrically actuated microvalve for liquid flow control,” *Journal of Microelectromechanical Systems*, vol. 15, no. 3, pp. 686–696, 2006.
- [244] J. Lv, Y. Jiang, D. Zhang, Y. Zhao, and X. Sun, “Characterization on the fatigue performance of a piezoelectric microvalve with a microfabricated silicon valve seat,” *Journal of Micromechanics and Microengineering*, vol. 24, no. 1, 2014.
- [245] M. Nafea, A. Nawabjan, and M. S. Mohamed Ali, “A wirelessly-controlled piezoelectric microvalve for regulated drug delivery,” *Sensors and Actuators, A: Physical*, vol. 279, pp. 191–203, 2018.
- [246] J. M. Park, R. P. Taylor, A. T. Evans, T. R. Brosten, G. F. Nellis, S. A. Klein, J. R. Feller, L. Salerno, and Y. B. Gianchandani, “A piezoelectric microvalve for cryogenic applications,” *Journal of Micromechanics and Microengineering*, vol. 18, no. 1, 2008.
- [247] M. Scheuenpflug, D. Guenther, F. Irlinger, and T. Lueth, “Microfluidic module system with piezo driven microvalve for synthesis of radiopharmaceutical products,” in *Annual International Conference of the*

- IEEE Engineering in Medicine and Biology - Proceedings*, 2007, pp. 5707–5710.
- [248] M. Scheuenpflug, D. Guenther, F. Irlinger, and T. Lueth, “Microfluidic module system with piezo driven microvalve for synthesis of radiopharmaceutical products,” *Conference proceedings: ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, pp. 5708–5711, 2007.
- [249] X. Wu, S.-H. Kim, C.-H. Ji, and M. G. Allen, “A solid hydraulically amplified piezoelectric microvalve,” *Journal of Micromechanics and Microengineering*, vol. 21, no. 9, 2011.
- [250] E.-H. Yang, C. Lee, and J. M. Khodadadi, “Development of MEMS-based piezoelectric microvalve technologies,” *Sensors and Materials*, vol. 19, no. 1, pp. 1–18, 2007.
- [251] S. Messner, M. Mueller, J. Schaible, H. Sandmaier, and R. Zengerle, “3-Way microvalve for pneumatic applications fabricated by silicon micromachining,” in *American Society of Mechanical Engineers, Dynamic Systems and Control Division (Publication) DSC*, 1998, vol. 66, pp. 159–164.
- [252] H. Jerman, “Electrically activated normally closed diaphragm valves,” *Journal of Micromechanics and Microengineering*, vol. 4, no. 4, pp. 210–216, 1994.
- [253] C. A. Rich and K. D. Wise, “A high-flow thermopneumatic microvalve with improved efficiency and integrated state sensing,” *Journal of Microelectromechanical Systems*, vol. 12, no. 2, pp. 201–208, 2003.
- [254] J.-H. Kim, K.-H. Na, C. J. Kang, D. Jeon, and Y.-S. Kim, “A disposable thermopneumatic-actuated microvalve stacked with PDMS layers and ITO-coated glass,” *Microelectronic Engineering*, vol. 73–74, pp. 864–869, 2004.
- [255] J.-C. Yoo, M.-C. Moon, C. J. Kang, and Y.-S. Kim, “Thermopneumatic-actuated PDMS microvalve and micropump integrated with the same fabrication process,” in *Digest of Technical Papers - International Conference on Solid State Sensors and Actuators and Microsystems, TRANSDUCERS '05*, 2005, vol. 1, pp. 664–667.
- [256] T. Aravind, S. Praveen Kumar, G. K. F. Raj, P. Prasanth, and P. S. Gobinath, “A novel thermopneumatic based micropump and microvalve using phase

- change liquid,” in *2013 IEEE International Conference on “Smart Structures and Systems”*, ICSSS 2013, 2013, pp. 66–69.
- [257] A. Pourmand, S. A. M. Shaegh, H. B. Ghavifekr, E. Najafi Aghdam, M. R. Dokmeci, A. Khademhosseini, and Y. S. Zhang, “Fabrication of whole-thermoplastic normally closed microvalve, micro check valve, and micropump,” *Sensors and Actuators, B: Chemical*, vol. 262, pp. 625–636, 2018.
- [258] A. Banejad, M. Passandideh-Fard, H. Niknam, M. J. Mirshojaeian Hosseini, and S. A. Mousavi Shaegh, “Design, fabrication and experimental characterization of whole-thermoplastic microvalves and micropumps having micromilled liquid channels of rectangular and half-elliptical cross-sections,” *Sensors and Actuators, A: Physical*, vol. 301, 2020.
- [259] S. Augustine, P. Gu, X. Zheng, T. Nishida, and Z. H. Fan, “Low-power electrically controlled thermoelastic microvalves integrated in thermoplastic microfluidic devices,” *Microfluidics and Nanofluidics*, vol. 19, no. 6, pp. 1385–1394, 2015.
- [260] H. Takehara, K. Uto, M. Ebara, T. Aoyagi, and T. Ichiki, “Shape-memory polymer microvalves,” in *Proceedings of the 16th International Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2012*, 2012, pp. 1846–1848.
- [261] C. Jiang, K. Uto, M. Ebara, T. Aoyagi, and T. Ichiki, “Implementation of poly($\hat{\mu}$ -caprolactone) sheet-based shape-memory polymer microvalves into plastic-based microfluidic devices,” *Japanese Journal of Applied Physics*, vol. 54, no. 6, 2015.
- [262] C. Jiang, H. Takehara, K. Uto, M. Ebara, T. Aoyagi, and T. Ichiki, “Evaluation of microvalves developed for point-of-care testing devices using shape-memory polymers,” *Journal of Photopolymer Science and Technology*, vol. 26, no. 5, pp. 581–585, 2013.
- [263] T. Grand, C. Megnin, J. Barth, and M. Kohl, “Batch fabrication of shape memory actuated polymer microvalves by transfer bonding techniques,” *Journal of Microelectronics and Electronic Packaging*, vol. 6, no. 4, pp. 219–227, 2009.

- [264] C. Megnin, B. Moradi, J. Zuern, H. Ossmer, M. Gueltig, and M. Kohl, "Shape memory alloy based controllable multi-port microvalve," *Microsystem Technologies*, vol. 26, no. 3, pp. 793–800, 2020.
- [265] C. Cheng, A. R. Nair, R. Thakur, and G. Fridman, "Normally closed plunger-membrane microvalve self-actuated electrically using a shape memory alloy wire," *Microfluidics and Nanofluidics*, vol. 22, no. 3, 2018.
- [266] C. Megnin and M. Kohl, "Shape memory alloy microvalves for a fluidic control system," *Journal of Micromechanics and Microengineering*, vol. 24, no. 2, 2014.
- [267] W.-Y. Liu, X.-T. Fu, X.-Q. Zhang, and W.-Y. Hu, "A new shape memory alloy microvalve based on surface acoustic wave," *Ferroelectrics*, vol. 504, no. 1, pp. 22–30, 2016.
- [268] R. Luharuka and P. J. Hesketh, "A bistable electromagnetically actuated rotary gate microvalve," *Journal of Micromechanics and Microengineering*, vol. 18, no. 3, 2008.
- [269] B. Wagner, H. J. Quenzer, S. Hoerschelmann, T. Lisec, and M. Juerss, "Bistable microvalve with pneumatically coupled membranes," in *Proceedings of the IEEE Micro Electro Mechanical Systems (MEMS)*, 1996, pp. 384–388.
- [270] B. Yang, B. Wang, and W. K. Schomburg, "A thermopneumatically actuated bistable microvalve," *Journal of Micromechanics and Microengineering*, vol. 20, no. 9, 2010.
- [271] C. Megnin, J. Barth, and M. Kohl, "A bistable SMA microvalve for 3/2-way control," *Sensors and Actuators, A: Physical*, vol. 188, pp. 285–291, 2012.
- [272] T. Watanabe, G. C. Biswas, E. T. Carlen, and H. Suzuki, "An autonomous electrochemically-actuated microvalve for controlled transport in stand-alone microfluidic systems," *RSC Advances*, vol. 7, no. 62, pp. 39018–39023, 2017.
- [273] C. Das and F. Payne, "Design and characterization of low power, low dead volume electrochemically-driven microvalve," *Sensors and Actuators, A: Physical*, vol. 241, pp. 104–112, 2016.
- [274] A. P. Washe, P. Lozano-Sánchez, D. Bejarano-Nosas, B. Teixeira-Dias, and I. Katakis, "Electrochemically actuated passive stop-go microvalves for flow control in microfluidic systems," *Microelectronic Engineering*, vol. 111, pp. 416–420, 2013.

- [275] S. Park, S. H. Um, and Y.-K. Kim, "Fabrication process for an electrochemical microfluidic chip containing a microvalve system," *Biochip Journal*, vol. 6, no. 4, pp. 372–378, 2012.
- [276] A. Ezkerra, L. J. Fernández, K. Mayora, and J. M. Ruano-López, "A microvalve for lab-on-a-chip applications based on electrochemically actuated SU8 cantilevers," *Sensors and Actuators, B: Chemical*, vol. 155, no. 2, pp. 505–511, 2011.
- [277] D. E. Lee, S. Soper, and W. Wang, "Design and fabrication of an electrochemically actuated microvalve," *Microsystem Technologies*, vol. 14, no. 9–11, pp. 1751–1756, 2008.
- [278] A. Ezkerra, L. J. Fernández, A. Wolff, K. Mayora, and J. M. Ruano-López, "Electrochemical bubble-actuated microvalves and peristaltic pumps based on embedded SU-8 microcantilevers," in *12th International Conference on Miniaturized Systems for Chemistry and Life Sciences - The Proceedings of MicroTAS 2008 Conference*, 2008, pp. 182–184.
- [279] S. Z. Hua, F. Sachs, and H. D. Chopra, "Electrochemically actuated microvalves for microfluidic systems," in *ASME International Mechanical Engineering Congress and Exposition, Proceedings*, 2002, pp. 507–512.
- [280] S. Rahimi, E. H. Sarraf, G. K. Wong, and K. Takahata, "Implantable drug delivery device using frequency-controlled wireless hydrogel microvalves," *Biomedical Microdevices*, vol. 13, no. 2, pp. 267–277, 2011.
- [281] M. Böcker, M. Raue, S. Schusser, C. Jeitner, L. Breuer, P. Wagner, A. Poghossian, A. Förster, T. Mang, and M. J. Schöning, "Microfluidic chip with integrated microvalves based on temperature- and pH-responsive hydrogel thin films," *Physica Status Solidi (A) Applications and Materials Science*, vol. 209, no. 5, pp. 839–845, 2012.
- [282] A. Baldi, Y. Gu, P. E. Loftness, R. A. Siegel, and B. Ziaie, "A hydrogel-actuated environmentally sensitive microvalve for active flow control," *Journal of Microelectromechanical Systems*, vol. 12, no. 5, pp. 613–621, 2003.
- [283] M. R. Bayat and M. Baghani, "Fully-Coupled Transient Fluid-Solid Interaction Simulation of the pH-Sensitive Hydrogel-Based Microvalve," *International Journal of Applied Mechanics*, vol. 11, no. 7, 2019.

- [284] C. Hu, M. Nakajima, T. Yue, M. Takeuchi, M. Seki, Q. Huang, and T. Fukuda, "On-chip fabrication of magnetic alginate hydrogel microfibers by multilayered pneumatic microvalves," *Microfluidics and Nanofluidics*, vol. 17, no. 3, pp. 457–468, 2014.
- [285] E. Lee, H. Lee, S. I. Yoo, and J. Yoon, "Photothermally triggered fast responding hydrogels incorporating a hydrophobic moiety for light-controlled microvalves," *ACS Applied Materials and Interfaces*, vol. 6, no. 19, pp. 16949–16955, 2014.
- [286] S. Lin, W. Wang, X.-J. Ju, R. Xie, and L.-Y. Chu, "A simple strategy for in situ fabrication of a smart hydrogel microvalve within microchannels for thermostatic control," *Lab on a Chip*, vol. 14, no. 15, pp. 2626–2634, 2014.
- [287] R. H. Liu, Q. Yu, and D. J. Beebe, "Fabrication and characterization of hydrogel-based microvalves," *Journal of Microelectromechanical Systems*, vol. 11, no. 1, pp. 45–53, 2002.
- [288] F. Obst, A. Beck, C. Bishayee, P. J. Mehner, A. Richter, B. Voit, and D. Appelhans, "Hydrogel microvalves as control elements for parallelized enzymatic cascade reactions in microfluidics," *Micromachines*, vol. 11, no. 2, 2020.
- [289] A. Richter, D. Kuckling, S. Howitz, T. Gehring, and K.-F. Arndt, "Electronically controllable microvalves based on smart hydrogels: Magnitudes and potential applications," *Journal of Microelectromechanical Systems*, vol. 12, no. 5, pp. 748–753, 2003.
- [290] Y. Shiraki, K. Tsuruta, J. Morimoto, C. Ohba, A. Kawamura, R. Yoshida, R. Kawano, T. Uragami, and T. Miyata, "Preparation of molecule-responsive microsized hydrogels via photopolymerization for smart microchannel microvalves," *Macromolecular Rapid Communications*, vol. 36, no. 6, pp. 515–519, 2015.
- [291] M. Tehranirokh, B. Y. Majlis, and B. Bais, "Design and simulation of a normally closed glucose sensitive hydrogel based microvalve," *Microsystem Technologies*, vol. 15, no. 5, pp. 753–762, 2009.
- [292] A. Voigt, U. Marschner, and A. Richter, "Multiphysics equivalent circuit of a thermally controlled hydrogel microvalve," *Journal of Intelligent Material Systems and Structures*, vol. 28, no. 16, pp. 2265–2274, 2017.

- [293] J. Zhang, P. Du, D. Xu, Y. Li, W. Peng, G. Zhang, F. Zhang, and X. Fan, “Near-Infrared Responsive MoS₂/Poly(N-isopropylacrylamide) Hydrogels for Remote Light-Controlled Microvalves,” *Industrial and Engineering Chemistry Research*, vol. 55, no. 16, pp. 4526–4531, 2016.
- [294] C.-H. Zhu, Y. Lu, J. Peng, J.-F. Chen, and S.-H. Yu, “Photothermally sensitive poly(N-isopropylacrylamide)/graphene oxide nanocomposite hydrogels as remote light-controlled liquid microvalves,” *Advanced Functional Materials*, vol. 22, no. 19, pp. 4017–4022, 2012.
- [295] J.-C. Yoo, Y. J. Choi, C. J. Kang, and Y.-S. Kim, “A novel polydimethylsiloxane microfluidic system including thermopneumatic-actuated micropump and Paraffin-actuated microvalve,” *Sensors and Actuators, A: Physical*, vol. 139, no. 1–2 SPEC. ISS., pp. 216–220, 2007.
- [296] B. Yang and Q. Lin, “A latchable microvalve using phase change of paraffin wax,” *Sensors and Actuators, A: Physical*, vol. 134, no. 1, pp. 194–200, 2007.
- [297] R. Pal, M. Yang, B. N. Johnson, D. T. Burke, and M. A. Burns, “Phase change microvalve for integrated devices,” *Analytical Chemistry*, vol. 76, no. 13, pp. 3740–3748, 2004.
- [298] B. Liu, J. Yang, J. Yang, D. Li, G. Gao, and Y. Wang, “A thermally actuated microvalve using paraffin composite by induction heating,” *Microsystem Technologies*, vol. 25, no. 10, pp. 3969–3975, 2019.
- [299] K. Kolari, T. Havia, I. Stuns, and K. Hjort, “Flow restrictor silicon membrane microvalve actuated by optically controlled paraffin phase transition,” *Journal of Micromechanics and Microengineering*, vol. 24, no. 8, 2014.
- [300] E. T. Carlen and C. H. Mastrangelo, “Surface micromachined paraffin-actuated microvalve,” *Journal of Microelectromechanical Systems*, vol. 11, no. 5, pp. 408–420, 2002.
- [301] J.-W. Kim, K. Yoshida, K. Kouda, and S. Yokota, “A flexible electro-rheological microvalve (FERV) based on SU-8 cantilever structures and its application to microactuators,” *Sensors and Actuators, A: Physical*, vol. 156, no. 2, pp. 366–372, 2009.
- [302] X. Niu, W. Wen, and Y.-K. Lee, “Electrorheological-fluid-based microvalves,” *Applied Physics Letters*, vol. 87, no. 24, pp. 1–3, 2005.

- [303] K. Yoshida, T. Takamatsu, Y. Yoneda, and S. Yokota, "A microvalve using magneto-rheological fluid," *Nihon Kikai Gakkai Ronbunshu, C Hen/Transactions of the Japan Society of Mechanical Engineers, Part C*, vol. 71, no. 4, pp. 1355–1360, 2005.
- [304] H. Takao and M. Ishida, "Pneumatic MEMS in-channel microvalves with in-plane control ports for micro fluidic systems integrated on a chip surface," *Sensors and Materials*, vol. 19, no. 1, pp. 19–34, 2007.
- [305] H. Takao, M. Ishida, and K. Sawada, "A pneumatically actuated full in-channel microvalve with MOSFET-like function in fluid channel networks," *Journal of Microelectromechanical Systems*, vol. 11, no. 5, pp. 421–426, 2002.
- [306] D. Satoh, S. Tanaka, and M. Esashi, "Electrostatically controlled, pneumatically actuated microvalve with low pressure loss," *IEEEJ Transactions on Electrical and Electronic Engineering*, vol. 3, no. 3, pp. 305–312, 2008.
- [307] F. Perdigones, A. Luque, and J. M. Quero, "Pneumatically actuated positive gain microvalve with n-channel metal-oxide semiconductor-like behaviour," *Micro and Nano Letters*, vol. 6, no. 6, pp. 363–365, 2011.
- [308] R. T. Kelly, C. Wang, S. J. Rausch, C. S. Lee, and K. Tang, "Pneumatic microvalve-based hydrodynamic sample injection for high-throughput, quantitative zone electrophoresis in capillaries," *Analytical Chemistry*, vol. 86, no. 13, pp. 6723–6729, 2014.
- [309] M. Kaminaga, T. Ishida, and T. Omata, "Fabrication of pneumatic microvalve for tall microchannel using inclined lithography," *Micromachines*, vol. 7, no. 12, 2016.
- [310] K. Hosokawa and R. Maeda, "Pneumatically-actuated three-way microvalve fabricated with polydimethylsiloxane using the membrane transfer technique," *Journal of Micromechanics and Microengineering*, vol. 10, no. 3, pp. 415–420, 2000.
- [311] G. Gunther and H.-J. Quenzer, "Development of a pneumatic microvalve [Entwicklung eines pneumatischen Mikroventils]," *Olhydraulik und Pneumatik*, vol. 44, no. 9, pp. 578–581, 2000.

- [312] G. Gunther, "Development of a pneumatic 3/2-way-microvalve [Entwicklung eines pneumatischen 3/2-Wege-Mikroventils]," *Olhydraulik und Pneumatik*, vol. 42, no. 6, pp. 396–398, 1998.
- [313] G. Günther, "Development of a microvalve for pneumatic applications [Mikroventile für die Pneumatik]," *Konstruktion*, no. 11–12, pp. 22–24, 1999.
- [314] Y. Cong, S. Katipamula, T. Geng, S. A. Prost, K. Tang, and R. T. Kelly, "Electrokinetic sample preconcentration and hydrodynamic sample injection for microchip electrophoresis using a pneumatic microvalve," *Electrophoresis*, vol. 37, no. 3, pp. 455–462, 2016.
- [315] H. Afrasiab, M. R. Movahhedy, and A. Assempour, "Finite element and analytical fluid-structure interaction analysis of the pneumatically actuated diaphragm microvalves," *Acta Mechanica*, vol. 222, no. 1–2, pp. 175–192, 2011.
- [316] S. J. Kim, H. Kim II, S. J. Park, and S. I. Kim, "Shape change characteristics of polymer hydrogel based on polyacrylic acid/poly(vinyl sulfonic acid) in electric fields," *Sensors and Actuators, A: Physical*, vol. 115, no. 1, pp. 146–150, 2004.
- [317] K. W. Oh and C. H. Ahn, "A review of microvalves," *Journal of Micromechanics and Microengineering*, vol. 16, no. 5, pp. R13–R39, 2006.
- [318] B. Alsaeed and F. R. Mansour, "Distance-based paper microfluidics; principle, technical aspects and applications," *Microchemical Journal*, vol. 155, 2020.
- [319] J. Gilmore, M. Islam, and R. Martinez-Duarte, "Challenges in the use of compact disc-based centrifugal microfluidics for healthcare diagnostics at the extreme point of care," *Micromachines*, vol. 7, no. 4, 2016.
- [320] B. Gao, X. Li, Y. Yang, J. Chu, and B. He, "Emerging paper microfluidic devices," *Analyst*, vol. 144, no. 22, pp. 6497–6511, 2019.
- [321] S. M. T. Delgado, D. J. Kinahan, N. A. Kilcawley, L. A. N. Julius, B. Henderson, J. G. Korvink, J. Ducree, and D. Mager, "A fully automated wirelessly powered centrifugal platform towards a sample-to-answer chemiluminescent ELISA assay for CVD detection," in *20th International Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2016*, 2016, pp. 1348–1349.

- [322] B. S. Lee, J.-N. Lee, J.-M. Park, J.-G. Lee, S. Kim, Y.-K. Cho, and C. Ko, “A fully automated immunoassay from whole blood on a disc,” *Lab Chip*, vol. 9, no. 11, pp. 1548–1555, 2009.
- [323] S. Lutz, P. Weber, M. Focke, B. Faltin, J. Hoffmann, C. Muller, D. Mark, G. Roth, P. Munday, N. Armes, O. Piepenburg, R. Zengerle, and F. Von Stetten, “Microfluidic lab-on-a-foil for nucleic acid analysis based on isothermal recombinase polymerase amplification (RPA),” *Lab Chip*, vol. 10, no. 7, pp. 887–893, 2010.
- [324] A. Rothert, S. K. Deo, L. Millner, L. G. Puckett, M. J. Madou, and S. Daunert, “Whole-cell-reporter-gene-based biosensing systems on a compact disk microfluidics platform,” *Anal. Biochem.*, vol. 342, no. 1, pp. 11–19, 2005.
- [325] A. Thiha and F. Ibrahim, “A colorimetric Enzyme-Linked Immunosorbent Assay (ELISA) detection platform for a point-of-care dengue detection system on a lab-on-compact-disc,” *Sensors*, vol. 15, no. 5, pp. 11431–11441, 2015.
- [326] A. S. Watts, A. A. Urbas, E. Moschou, V. G. Gavalas, J. V. Zoval, M. Madou, and L. G. Bachas, “Centrifugal microfluidics with integrated sensing microdome optodes for multiion detection,” *Anal Chem*, vol. 79, no. 21, pp. 8046–8054, 2007.
- [327] D. Mark, P. Weber, S. Lutz, M. Focke, R. Zengerle, and F. Von Stetten, “Aliquoting on the centrifugal microfluidic platform based on centrifugo-pneumatic valves,” *Microfluid. Nanofluid.*, vol. 10, no. 6, pp. 1279–1288, 2011.
- [328] Y.-S. Park, V. Sunkara, Y. Kim, W. S. Lee, J.-R. Han, and Y.-K. Cho, “Fully automated centrifugal microfluidic device for ultrasensitive protein detection from whole blood,” *J. Vis. Exp.*, vol. 2016, no. 110, 2016.
- [329] W. Al-Faqheri, F. Ibrahim, T. H. G. Thio, N. Bahari, H. Arof, H. A. Rothan, R. Yusof, and M. Madou, “Development of a passive liquid valve (PLV) utilizing a pressure equilibrium phenomenon on the centrifugal microfluidic platform,” *Sensors*, vol. 15, no. 3, pp. 4658–4676, 2015.
- [330] J. Gaughran, D. Kinahan, R. Mishra, and J. Ducree, “Solvent-selective membranes for automating sequential liquid release and routing of nucleic acid purification protocols on a simple spindle motor,” in *20th International*

Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2016, 2016, pp. 876–877.

- [331] M. Kitsara, C. E. Nwankire, L. Walsh, G. Hughes, M. Somers, D. Kurzbuch, X. Zhang, G. G. Donohoe, R. O’Kennedy, and J. Ducree, “Spin coating of hydrophilic polymeric films for enhanced centrifugal flow control by serial siphoning,” *Microfluid. Nanofluid.*, vol. 16, no. 4, pp. 691–699, 2014.
- [332] F. Schwemmer, T. Hutzenlaub, D. Buselmeier, N. Paust, F. Von Stetten, D. Mark, R. Zengerle, and D. Kosse, “Centrifugo-pneumatic multi-liquid aliquoting - Parallel aliquoting and combination of multiple liquids in centrifugal microfluidics,” *Lab Chip*, vol. 15, no. 15, pp. 3250–3258, 2015.
- [333] S. Soroori, J. M. Rodriguez-Delgado, H. Kido, G. Dieck-Assad, M. Madou, and L. Kulinsky, “The use of polybutene for controlling the flow of liquids in centrifugal microfluidic systems,” *Microfluid. Nanofluid.*, vol. 20, no. 1, pp. 1–13, 2016.
- [334] D. Carpentras, L. Kulinsky, and M. Madou, “A Novel Magnetic Active Valve for Lab-on-CD Technology,” *J Microelectromech S*, vol. 24, no. 5, pp. 1322–1330, 2015.
- [335] Z. Noroozi, H. Kido, and M. J. Madou, “Electrolysis-induced pneumatic pressure for control of liquids in a centrifugal system,” *J Electrochem Soc*, vol. 158, no. 11, pp. P130–P135, 2011.
- [336] L. Swayne, A. Kazarine, E. J. Templeton, and E. D. Salin, “Rapid prototyping of pneumatically actuated hydrocarbon gel valves for centrifugal microfluidic devices,” *Talanta*, vol. 134, pp. 443–447, 2015.
- [337] M. Amasia, M. Cozzens, and M. J. Madou, “Centrifugal microfluidic platform for rapid PCR amplification using integrated thermoelectric heating and ice-valving,” *Sens. Actuators, B*, vol. 161, no. 1, pp. 1191–1197, 2012.
- [338] S. Sugiura, A. SzilÁgyi, K. Sumaru, K. Hattori, T. Takagi, G. Filipcsei, M. ZrÁnyi, and T. Kanamori, “On-demand microfluidic control by micropatterned light irradiation of a photoresponsive hydrogel sheet,” *Lab Chip*, vol. 9, no. 2, pp. 196–198, 2009.
- [339] K. Abi-Samra, M. R. cand Madou Hanson, and R. A. Gorkin III, “Infrared controlled waxes for liquid handling and storage on a CD-microfluidic platform,” *Lab Chip*, vol. 11, no. 4, pp. 723–726, 2011.

- [340] S. S. Mohan, M. del Mar Hershenson, S. P. Boyd, and T. H. Lee, “Simple accurate expressions for planar spiral inductances,” *IEEE Journal of Solid-State Circuits*, vol. 34, no. 10, pp. 1419–1424, 1999.
- [341] M. S. Mohamed Ali, “Integration and wireless control methods for micromachined shape-memory-alloy actuators and their MEMS applications,” University of British Columbia, 2012.
- [342] A. Fick, “Ueber Diffusion,” *Annalen der Physik*, vol. 170, no. 1, pp. 59–86, 1855.
- [343] M. A. Zainal, S. Sahlan, and M. S. Mohamed Ali, “Micromachined shape-memory-alloy microactuators and their application in biomedical devices,” *Micromachines*, vol. 6, no. 7, pp. 879–901, 2015.
- [344] M. A. Zainal, P. S. Chee, and M. S. M. Ali, “Wireless valving for centrifugal microfluidic platform using field frequency modulation,” in *Proceedings of the IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, 2017, pp. 1351–1354.
- [345] M. A. Zainal, Y. M. Yunos, R. A. Rahim, and M. S. Mohamed Ali, “Wireless valving for centrifugal microfluidic disc,” *Journal of Microelectromechanical Systems*, vol. 26, no. 6, pp. 1327–1334, 2017.
- [346] M. A. Zainal, A. Ahmad, and M. S. Mohamed Ali, “Frequency-controlled wireless shape memory polymer microactuator for drug delivery application,” *Biomedical Microdevices*, vol. 19, no. 1, 2017.
- [347] M. A. Zainal and M. S. Mohamed Ali, “Wireless shape memory polymer microactuator for implantable drug delivery application,” in *IECBES 2016 - IEEE-EMBS Conference on Biomedical Engineering and Sciences*, 2016, pp. 76–79.

LIST OF PUBLICATIONS

Journals

- M. A. Zainal, S. Sahlan, and M. S. Mohamed Ali, “Micromachined shape-memory-alloy microactuators and their application in biomedical devices,” *Micromachines*, vol. 6, no. 7, pp. 879–901, 2015. (Part of Chapter 2)
- M. A. Zainal, A. Ahmad, and M. S. Mohamed Ali, “Frequency-controlled wireless shape memory polymer microactuator for drug delivery application,” *Biomedical Microdevices*, vol. 19, no. 1, 2017. (Part of Chapter 2,3 and 4)
- M. A. Zainal, Y. M. Yunos, R. A. Rahim, and M. S. Mohamed Ali, “Wireless valving for centrifugal microfluidic disc,” *Journal of Microelectromechanical Systems*, vol. 26, no. 6, pp. 1327–1334, 2017. (Part of Chapter 2,3 and 5)

Conferences

- M. A. Zainal and M. S. Mohamed Ali, “Wireless shape memory polymer microactuator for implantable drug delivery application,” in *IECBES 2016 - IEEE-EMBS Conference on Biomedical Engineering and Sciences*, 2016, pp. 76–79. (Part of Chapter 2,3 and 4)
- M. A. Zainal, P. S. Chee, and M. S. M. Ali, “Wireless valving for centrifugal microfluidic platform using field frequency modulation,” in *Proceedings of the IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, 2017, pp. 1351–1354.