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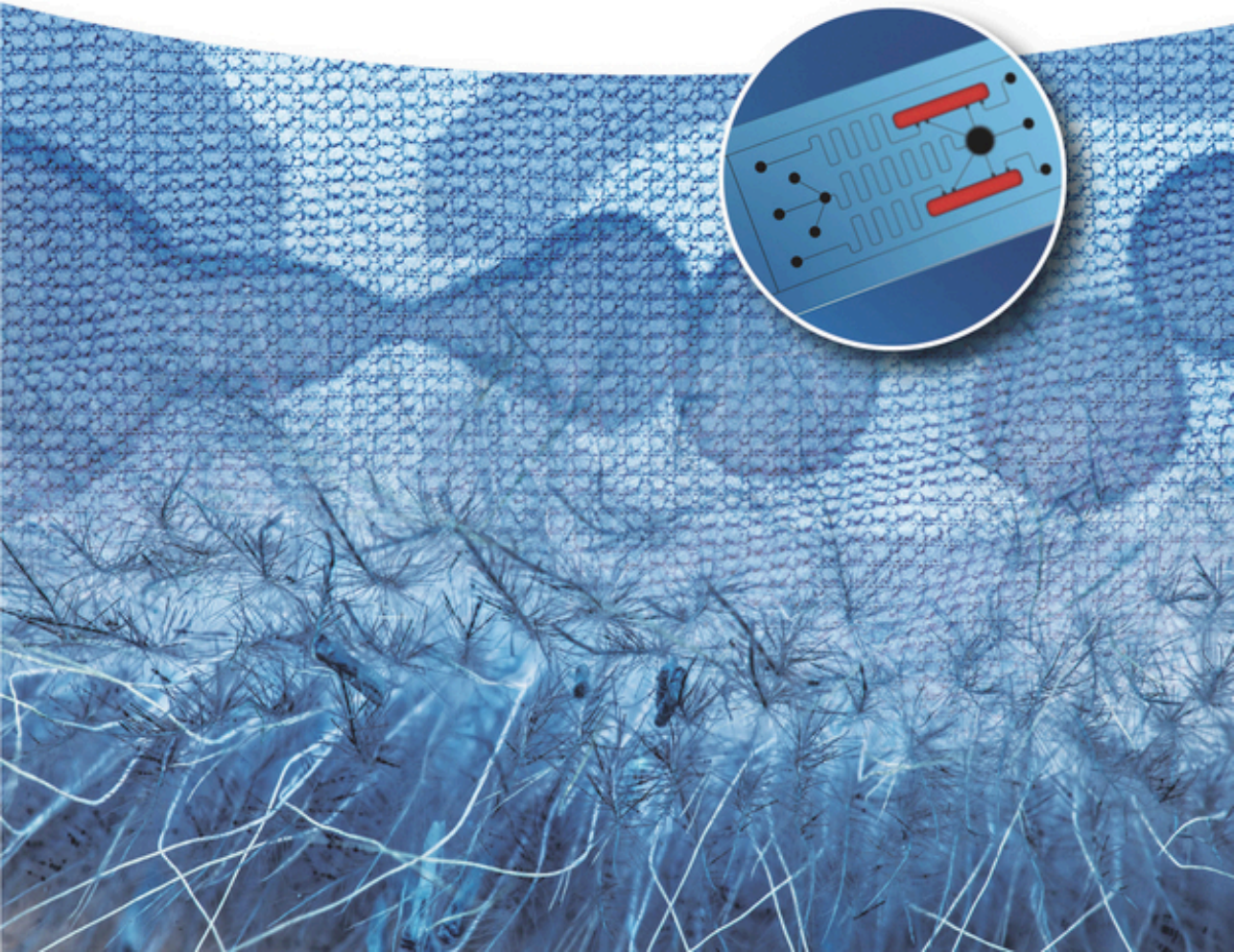
Microfluidics for Advanced Functional Polymeric Materials



Microfluidics for Advanced Functional Polymeric Materials

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WILEY-VCH

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Contents

Preface *xiii*

1 Introduction *1*
1.1 Microfluidics and Its Superiority in Controllable Fabrication of Functional Materials *1*
1.2 Microfluidic Fabrication of Microspheres and Microcapsules from Microscale Closed Liquid–Liquid Interfaces *3*
1.3 Microfluidic Fabrication of Membranes in Microchannels from Microscale Nonclosed Layered Laminar Interfaces *4*
1.4 Microfluidic Fabrication of Microfiber Materials from Microscale Nonclosed Annular Laminar Interfaces *5*
References *6*

2 Shear-Induced Generation of Controllable Multiple Emulsions in Microfluidic Devices *11*
2.1 Introduction *11*
2.2 Microfluidic Strategy for Shear-Induced Generation of Controllable Emulsion Droplets *12*
2.3 Shear-Induced Generation of Controllable Monodisperse Single Emulsions *14*
2.4 Shear-Induced Generation of Controllable Multiple Emulsions *16*
2.4.1 Shear-Induced Generation of Controllable Double Emulsions *16*
2.4.2 Shear-Induced Generation of Controllable Triple Emulsions *19*
2.5 Shear-Induced Generation of Controllable Multicomponent Multiple Emulsions *22*
2.5.1 Shear-Induced Generation of Controllable Quadruple-Component Double Emulsions *22*
2.5.2 Extended Microfluidic Device for Controllable Generation of More Complex Multicomponent Multiple Emulsions *27*
2.6 Summary *31*
References *31*

3 Wetting-Induced Generation of Controllable Multiple Emulsions in Microfluidic Devices *35*
3.1 Introduction *35*
3.2 Microfluidic Strategy for Wetting-Induced Production of Controllable Emulsions *36*
3.2.1 Strategy for Wetting-Induced Production of Controllable Emulsions via Wetting-Induced Spreading *36*
3.2.2 Strategy for Wetting-Induced Production of Controllable Emulsions via Wetting-Induced Coalescing *37*
3.3 Generation of Controllable Multiple Emulsions via Wetting-Induced Spreading *38*
3.3.1 Wetting-Induced Generation of Monodisperse Controllable Double Emulsions *38*
3.3.2 Wetting-Induced Generation of Monodisperse Higher Order Multiple Emulsions *41*
3.3.3 Wetting-Induced Generation of Monodisperse Multiple Emulsions via Droplet-Triggered Droplet Pairing *44*
3.4 Generation of Controllable Multiple Emulsions via Wetting-Induced Droplet Coalescing *47*
3.5 Summary *50*
References *52*

4 Microfluidic Fabrication of Monodisperse Hydrogel Microparticles *55*
4.1 Introduction *55*
4.2 Microfluidic Fabrication of Monodisperse PNIPAM Hydrogel Microparticles for Sensing Tannic Acid (TA) *55*
4.2.1 Microfluidic Fabrication of Monodisperse PNIPAM Hydrogel Microparticles *56*
4.2.2 Volume-Phase Transition Behaviors of PNIPAM Microgels Induced by TA *57*
4.3 Microfluidic Fabrication of Monodisperse Core–Shell PNIPAM Hydrogel Microparticles for Sensing Ethyl Gallate (EG) *62*
4.3.1 Microfluidic Fabrication of Monodisperse Core–Shell PNIPAM Hydrogel Microparticles *62*
4.3.2 Thermo-Responsive Phase Transition Behaviors of PNIPAM Microspheres in EG Solution *65*
4.3.3 The Intact-to-Broken Transformation Behaviors of Core–Shell PNIPAM Microcapsules in Aqueous Solution with Varying EG Concentrations *65*
4.4 Microfluidic Fabrication of Monodisperse Core–Shell Hydrogel Microparticles for the Adsorption and Separation of Pb^{2+} *67*
4.4.1 Microfluidic Fabrication of Monodisperse Core–Shell Microparticles with Magnetic Core and Hydrogel Shell *68*

4.4.2 Pb^{2+} Adsorption Behaviors of Magnetic PNB Core–Shell Microspheres *71*
4.5 Summary *75*
References *76*

5 Microfluidic Fabrication of Monodisperse Porous Microparticles *79*
5.1 Introduction *79*
5.2 Microfluidic Fabrication of Monodisperse Porous Poly(HEMA-MMA) Microparticles *79*
5.2.1 Microfluidic Fabrication Strategy *80*
5.2.2 Structures of Poly(HEMA-MMA) Porous Microspheres *82*
5.3 Microfluidic Fabrication of Porous PNIPAM Microparticles with Tunable Response Behaviors *83*
5.3.1 Microfluidic Fabrication Strategy *86*
5.3.2 Tunable Response Behaviors of Porous PNIPAM Microparticles *87*
5.4 Microfluidic Fabrication of PNIPAM Microparticles with Open-Celled Porous Structure for Fast Response *90*
5.4.1 Microfluidic Fabrication Strategy *91*
5.4.2 Morphologies and Microstructures of Porous PNIPAM Microparticles *93*
5.4.3 Thermo-Responsive Volume Change Behaviors of PNIPAM Porous Microparticles *98*
5.5 Summary *103*
References *103*

6 Microfluidic Fabrication of Uniform Hierarchical Porous Microparticles *105*
6.1 Introduction *105*
6.2 Microfluidic Strategy for Fabrication of Uniform Hierarchical Porous Microparticles *106*
6.3 Controllable Microfluidic Fabrication of Uniform Hierarchical Porous Microparticles *108*
6.3.1 Preparation of Hierarchical Porous Microparticles *108*
6.3.2 Hierarchical Porous Microparticles with Micrometer-Sized Pores from Deformed W/O/W Emulsions *108*
6.3.3 Integration of Nanometer- and Micrometer-Sized Pores for Creating Hierarchical Porous Microparticles *111*
6.4 Hierarchical Porous Microparticles for Oil Removal *114*
6.4.1 Concept of the Hierarchical Porous Microparticles for Oil Removal *114*
6.4.2 Hierarchical Porous Microparticles for Magnetic-Guided Oil Removal *115*
6.5 Hierarchical Porous Microparticles for Protein Adsorption *116*

6.5.1 Concept of Hierarchical Porous Microparticles for Protein Adsorption *116*
6.5.2 Hierarchical Porous Microparticles for Enhanced Protein Adsorption *117*
6.6 Summary *118*
References *118*

7 Microfluidic Fabrication of Monodisperse Hollow Microcapsules *123*
7.1 Introduction *123*
7.2 Microfluidic Fabrication of Monodisperse Ethyl Cellulose Hollow Microcapsules *124*
7.2.1 Microfluidic Fabrication Strategy *124*
7.2.2 Morphologies and Structures of Ethyl Cellulose Hollow Microcapsules *125*
7.3 Microfluidic Fabrication of Monodisperse Calcium Alginate Hollow Microcapsules *131*
7.3.1 Microfluidic Fabrication Strategy *132*
7.3.2 Morphologies and Structures of Calcium Alginate Hollow Microcapsules *133*
7.4 Microfluidic Fabrication of Monodisperse Glucose-Responsive Hollow Microcapsules *136*
7.4.1 Microfluidic Fabrication Strategy *136*
7.4.2 Glucose-Responsive Behaviors of Microcapsules *140*
7.4.3 Glucose-Responsive Drug Release Behaviors of Microcapsules *142*
7.5 Microfluidic Fabrication of Monodisperse Multi-Stimuli-Responsive Hollow Microcapsules *144*
7.5.1 Microfluidic Fabrication Strategy *145*
7.5.2 Stimuli-Responsive Behaviors of Microcapsules *150*
7.5.3 Controlled-Release Characteristics of Multi-Stimuli-Responsive Microcapsules *154*
7.6 Summary *158*
References *158*

8 Microfluidic Fabrication of Monodisperse Core–Shell Microcapsules *161*
8.1 Introduction *161*
8.2 Microfluidic Strategy for Fabrication of Monodisperse Core–Shell Microcapsules *162*
8.3 Smart Core–Shell Microcapsules for Thermo-Triggered Burst Release *162*
8.3.1 Fabrication of Core–Shell Microcapsules for Thermo-Triggered Burst Release of Oil-Soluble Substances *162*
8.3.2 Fabrication of Core–Shell Microcapsules for Thermo-Triggered Burst Release of Nanoparticles *166*
8.3.3 Fabrication of Core–Shell Microcapsules for Direction-Specific Thermo-Responsive Burst Release *168*

8.4 Smart Core–Shell Microcapsules for Alcohol-Responsive Burst Release *171*
8.5 Smart Core–Shell Microcapsules for K^+-Responsive Burst Release *174*
8.6 Smart Core–Shell Microcapsules for pH-Responsive Burst Release *176*
8.6.1 Concept of the Core–Shell Microcapsules for pH-Responsive Burst Release *176*
8.6.2 Fabrication of the Core–Shell Chitosan Microcapsules *177*
8.6.3 Core–Shell Chitosan Microcapsules for pH-Responsive Burst Release *179*
8.7 Summary *182*
References *183*

9 Microfluidic Fabrication of Monodisperse Hole–Shell Microparticles *187*
9.1 Introduction *187*
9.2 Microfluidic Strategy for Fabrication of Monodisperse Hole–Shell Microparticles *188*
9.3 Hole–Shell Microparticles for Thermo-Driven Crawling Movement *188*
9.3.1 Concept of the Hole–Shell Microparticles for Thermo-Driven Crawling Movement *188*
9.3.2 Fabrication of Hole–Shell Microparticles for Thermo-Driven Crawling Movement *190*
9.3.3 Effect of Inner Cavity on the Thermo-Responsive Volume-Phase Transition Behaviors of Hole–Shell Microparticles *191*
9.3.4 Hole–Shell Microparticles for Thermo-Driven Crawling Movement *193*
9.4 Hole–Shell Microparticles for Pb^{2+} Sensing and Actuating *195*
9.4.1 Fabrication of Hole–Shell Microparticles for Pb^{2+} Sensing and Actuating *195*
9.4.2 Magnetic-Guided Targeting Behavior of Poly(NIPAM-*co*-B18C6Am) Hole–Shell Microparticles *195*
9.4.3 Effects of Pb^{2+} on the Thermo-Responsive Volume Change Behaviors of Poly(NIPAM-*co*-B18C6Am) Hole–Shell Microparticles *196*
9.4.4 Effects of Hollow Cavity on the Time-Dependent Volume Change Behaviors of Poly(NIPAM-*co*-B18C6Am) Hole–Shell Microparticles *199*
9.4.5 Micromanipulation of Poly(NIPAM-*co*-B18C6Am) Hole–Shell Microparticles for Preventing Pb^{2+} Leakage from Microcapillary *200*
9.5 Hole–Shell Microparticles for Controlled Capture and Confined Microreaction *201*
9.5.1 Microfluidic Fabrication of Hole–Shell Microparticles *201*
9.5.2 Precise Control over the Hole–Shell Structure of the Microparticles *203*
9.5.3 Precise Control over the Functionality of Hollow Core Surface *205*

9.5.4 Hole–Shell Microparticles for Controlled Capture and Confined Microreaction *206*
9.6 Summary *207*
References *207*

10 Microfluidic Fabrication of Controllable Multicompartmental Microparticles *211*
10.1 Introduction *211*
10.2 Microfluidic Strategy for the Fabrication of Controllable Multicompartmental Microparticles *212*
10.3 Multi-core/Shell Microparticles for Co-encapsulation and Synergistic Release *212*
10.3.1 Microfluidic Fabrication of Multi-core/Shell Microparticles *212*
10.3.2 Multi-core/Shell Microparticles for Controllable Co-encapsulation *213*
10.3.3 Multi-core/Shell Microparticles for Synergistic Release *216*
10.4 Trojan-Horse-Like Microparticles for Co-delivery and Programmed Release *217*
10.4.1 Fabrication of Trojan-Horse-Like Microparticles from Triple Emulsions *217*
10.5 Summary *218*
References *219*

11 Microfluidic Fabrication of Functional Microfibers with Controllable Internals *223*
11.1 Introduction *223*
11.2 Microfluidic Strategy for Fabrication of Functional Microfibers with Controllable Internals *224*
11.3 Core–Sheath Microfibers with Tubular Internals for Encapsulation of Phase Change Materials *224*
11.3.1 Fabrication of Core–Sheath Microfibers with Tubular Internals *224*
11.3.2 Morphological Characterization of the Core–Sheath Microfibers *227*
11.3.3 Thermal Property of the Core–Sheath Microfibers *227*
11.3.4 Core–Sheath Microfibers for Temperature Regulation *230*
11.4 Peapod-Like Microfibers with Multicompartmental Internals for Synergistic Encapsulation *235*
11.4.1 Fabrication of Peapod-Like Microfibers with Multicompartmental Internals *236*
11.4.2 Effects of Flow Rates on the Structures of Peapod-Like Jet Templates and Chitosan Microfibers *236*
11.4.3 Peapod-Like Chitosan Microfibers with Multicompartment Internals for Synergistic Encapsulation *240*
11.5 Spider-Silk-Like Microfibers with Spindle-Knot Internals for 3D Assembly and Water Collection *241*
11.5.1 Fabrication of Spider-Silk-Like Microfibers with Spindle-Knot Internals *241*

11.5.2 Morphological Characterization of the Jet Templates and Spider-Silk-Like Microfibers *242*
11.5.3 Magnetic-Guided Patterning and Assembling of the Ca-Alginate Microfibers *244*
11.5.4 Water Collection of Dehydrated Ca-Alginate Microfibers with Magnetic Spindle-Knot Internals *246*
11.6 Summary *248*
References *248*

12 Microfluidic Fabrication of Membrane-in-a-Chip with Self-Regulated Permeability *253*
12.1 Introduction *253*
12.2 Microfluidic Strategy for Fabrication of Membrane-in-a-Chip *254*
12.3 Temperature- and Ethanol-Responsive Smart Membrane in Microchip for Detection *255*
12.3.1 Fabrication of Nanogel-Containing Smart Membrane in Microchip *255*
12.3.2 Temperature-Responsive Self-Regulation of the Membrane Permeability *257*
12.3.3 Ethanol-Responsive Self-Regulation of the Membrane Permeability *260*
12.3.4 Reversible and Repeated Thermo/Ethanol-Responsive Self-Regulation of the Membrane Permeability *263*
12.4 Summary *264*
References *264*

13 Microfluidic Fabrication of Microvalve-in-a-Chip *267*
13.1 Introduction *267*
13.2 Microfluidic Strategy for Fabrication of Microvalve-in-a-Chip *268*
13.2.1 Fabrication of Thermo-Responsive Hydrogel Microvalve within Microchip for Thermostatic Control *268*
13.2.2 Fabrication of Pb^{2+}-Responsive Hydrogel Microvalve within Microchip for Pb^{2+} Detection *270*
13.3 Smart Microvalve-in-a-Chip with Thermostatic Control for Cell Culture *272*
13.3.1 Setup of Microvalve-Integrated Micro-heat-Exchanging System *273*
13.3.2 Thermo-Responsive Switch Performance of Hydrogel Microvalve *274*
13.3.3 Sealing Performance of Hydrogel Microvalve *276*
13.3.4 Temperature Self-Regulation of Hydrogel Microvalve for Thermostatic Control *277*
13.3.5 Temperature Self-Regulation with Hydrogel Microvalve for Cell Culture *279*
13.4 Smart Microvalve-in-a-Chip with Ultrasensitivity for Real-Time Detection *281*
13.4.1 Concept of the Microchip Incorporated with Pb^{2+}-Responsive Microgel for Real-Time Online Detection of Trace Pb^{2+} *281*
13.4.2 Sensitivity of the Pb^{2+} Detection Platform *283*

13.4.3 Selectivity and Repeatability of the Pb^{2+} Detection Platform *284*
13.4.4 Setup of Pb^{2+} Detection System for Real-Time Online Detection of Pb^{2+} in Tap Water for Pollution Warning *287*
13.4.5 Setup of Pb^{2+} Detection System for Real-Time Online Detection of Pb^{2+} in Wastewater from a Model Industrial Factory for Pollution Warning and Terminating *289*
13.5 Summary *289*
References *289*

14 Summary and Perspective *295*
14.1 Summary *295*
14.2 Perspective *295*
References *297*

Index *299*

Preface

Microfluidics, or the so-called lab-on-a-chip, has emerged as a distinct new technology since the beginning of the 1990s. The dimensions of the microfluidic channels and components are tens to hundreds of micrometers. The microfluidic devices can be used to flexibly manipulate the flow of microvolume fluids in microchannels, which are considered putting the lab on a chip. Due to the trend of miniaturization and integration of modern scientific and technological development, microfluidic technology has been widely concerned and valued by the international scientific and industrial communities. Since microfluidic technology can accurately manipulate small-volume fluids, it is rapidly extending from the original analytical chemistry platform for microanalysis and microdetection to high-throughput drug screening, micromixing, microreaction, microseparation, and so on. Due to its excellent ability to control fluid interfaces as well as excellent heat and mass transfer performances, microfluidic technology has become a novel and promising material preparation technology platform. Microfluidic technology has emerged in the construction of precisely controllable microstructured new functional materials with high performances and especially shows incomparable creativity and superiority compared with traditional technology in the design and preparation of some new functional materials with high added values.

This book, entitled *Microfluidics for Advanced Functional Polymeric Materials*, comprehensively and systematically treats modern understanding of the microfluidic technique and its great power in controllable fabrication of advanced functional polymeric materials. The contents range from the design and fabrication of microfluidic devices, the fundamentals and strategies for controllable microfluidic generation of multiphase liquid systems (e.g., discrete multiple emulsions and continuous laminar multiflow systems), and the use of these liquid systems with elaborate combination of their structures and compositions for controllable fabrication of advanced functional polymeric materials (e.g., solid microparticles, porous microparticles, hollow microcapsules, core–shell microcapsules, hole–shell microcapsules, multicompartmental microcapsules, microfibers, in-chip membranes, and microvalves). All the chapters together clearly describe the design concepts and fabrication strategies of advanced functional polymeric materials with microfluidics by combining the structures with the compositions of multiphase liquid systems to achieve advanced and novel functions. Vivid schematics and illustrations throughout

the book enhance the accessibility to the relevant theory and technologies. This book aims to be a definitive reference book for a wide general readership including chemists, chemical engineers, materials researchers, pharmaceutical scientists, biomedical researchers, and students in the related fields.

The book is composed of 14 chapters. In Chapter 1, a brief introduction of the superiority and potential of microfluidics in the construction of microscale phase interfaces and preparation of novel functional materials are briefly introduced. In Chapters 2 and 3, microfluidic strategies for shear-induced and wetting-induced generations of controllable multiple emulsions are introduced, respectively. In Chapters 4–6, microfluidic strategies for controllable fabrication of monodisperse hydrogel microparticles, porous microparticles, and hierarchical porous microparticles are introduced, respectively. In Chapters 7 and 8, microfluidic strategies for controllable fabrication of monodisperse hollow microcapsules and core–shell microcapsules with an oil core and a stimuli-responsive hydrogel shell are introduced, respectively. In Chapter 9, the microfluidic strategies for fabrication of controllable hole–shell microparticles from double emulsions are introduced. In Chapter 10, a microfluidic strategy for template synthesis of multicompartmental microparticles, with accurate control over the structures of their inner compartments and the encapsulation characteristics of their loaded contents, is introduced. In Chapter 11, simple and versatile microfluidic strategies for controllable fabrication of functional microfibers with tubular, peapod-like, and spindle-knot-like internals are introduced. In Chapter 12, a microfluidic strategy for *in situ* fabrication of nanogel-containing smart membranes in the microchannel of microchips is introduced. In Chapter 13, fabrication and performance of microchips incorporated with smart hydrogel microvalves for thermostatic control and trace analytes detection are introduced. Finally, perspectives on the microfluidic fabrication of advanced functional polymeric materials are given in Chapter 14.

The authors' group at Sichuan University (group website: http://teacher.scu.edu.cn/ftp_teacher0/cly/) has been devoted to the microfluidic fabrications of polymeric functional materials since 2006. In the past decade, they have made significant contributions to the development of this field. Most of the contents in this book are the fresh achievements of the authors' group on advanced functional materials fabricated with microfluidics. Prof. Liang-Yin Chu wrote Chapters 1, 4, 5, 7, 12, and 14, and Prof. Wei Wang wrote Chapters 2, 3, 6, 8–11, and 13. The authors are very grateful to Prof. David A. Weitz at Harvard University who helped the authors a lot to carry out investigations in the field of microfluidics. The authors would like to thank all the current and former group members who contributed to the investigations on microfluidics, especially Prof. Rui Xie, Prof. Xiao-Jie Ju, Prof. Zhuang Liu, Dr Li Liu, Dr Nan-Nan Deng, Dr Mao-Jie Zhang, Dr Zhi-Jun Meng, Dr Ya-Lan Yu, Dr Jie Wei, Dr Lei Zhang, Dr Chuan-Lin Mou, Dr Li-Li Yue, Dr Gang Chen, Dr Ying-Mei Liu, Dr Hai-Rong Yu, Dr Xiao-Heng He, Dr Ming-Yue Jiang, Dr Shuo Lin, Dr Fang Wu, Dr Xiao-Yi Zou, Jian Sun, Hao Zhang, Ping-Wei Ren, Jian-Ping Yang, Shuo-Wei Pi, Xi Lin, Guo-Qing Wen, Yi-Meng Sun, Chao Yang, Wei-Chao Zheng, Mei Yuan, Xiu-Lan Yang, and Ming Li, for their creative researches on microfluidics. The authors gratefully acknowledge all the professors, friends, and colleagues who helped the authors' group

to carry out investigations on microfluidics, and thank all the organizations who financially supported the authors' group for the continuous study in the field of microfluidics.

Finally, the authors would like to acknowledge the kind help of Dr Lifen Yang and the editorial staff at Wiley during the preparation and publication of this book.

September 2016

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1

Introduction

1.1 Microfluidics and Its Superiority in Controllable Fabrication of Functional Materials

Microfluidics, or the so-called lab-on-a-chip, has emerged as a distinct new technology since the beginning of 1990s [1]. The dimensions of the microfluidic channels and components are tens to hundreds of micrometers. The microfluidic devices can be used to flexibly manipulate the flow of microvolume fluids in microchannels, which are considered putting the lab on a chip (Figure 1.1). Due to the trend of miniaturization and integration of modern scientific and technological civilization development, microfluidic technology has been widely concerned and valued by the international scientific and industrial communities. In 2006, *Nature* magazine published a special issue on the topic of "*Insight: lab on a chip*," including seven related review papers [1, 2], where the editorial says that it might have the potential to become "a technology for this century." In 2010, *Chemical Society Reviews* published a special issue on the topic of "*From microfluidic applications to nanofluidic phenomena*," including 20 related review papers [3], which shows the promising momentum of development of microfluidic technologies. Since microfluidic technology can accurately manipulate small-volume fluids, it is rapidly extending from the original analytical chemistry platform for microanalysis and microdetection, to high-throughput drug screening, micromixing, microreaction, microseparation, and so on. Due to its excellent ability to control fluid interfaces as well as excellent heat and mass transfer performances, microfluidic technology has become a novel and promising material preparation technology platform (Figure 1.2). Microfluidic technology has emerged in the construction of precisely controllable microstructured new functional materials with high performances, such as microcapsules and microspheres, membranes in microchannels, and superfine fiber materials, and especially shows incomparable creativity and superiority compared with traditional technology in design and preparation of some new functional materials with high added values [4–35].

To sum up, stable phase interface structures of immiscible liquid phase systems that are constructed by the microfluidic technology can be mainly divided into two systems [4]: one is the emulsion droplet system with closed liquid–liquid interfaces, and the second is the laminar flow system with closed

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Figure 1.1 Microfluidics: putting the lab on a chip.

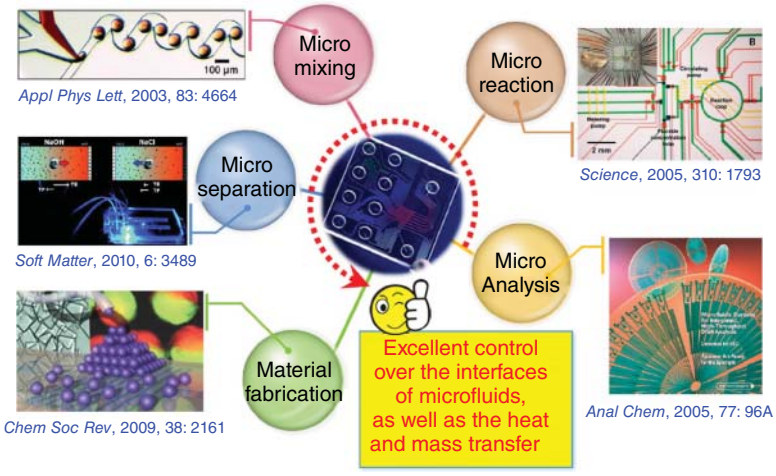

Figure 1.2 Microfluidic technology is becoming a novel technology platform for materials preparation because of its excellent control over the microfluid interfaces as well as the heat and mass transfer.

liquid–liquid interfaces (Figure 1.3). These two microfluidic-constructed stable phase interface structure systems can be used to prepare three categories of high-performance functional materials with accurate and controllable microstructures as follows [4–35]: (i) controllable fabrication of novel microspheres and microcapsules with precise microstructures by using emulsion droplet systems with closed phase interfaces as templates [4, 5, 7–32]; (ii) controllable fabrication of membranes in microchannels by using laminar flow systems with nonclosed layered phase interfaces [6, 33, 36, 37]; and (iii) controllable fabrication of novel microfiber materials by using laminar flow systems with nonclosed annular phase interfaces [4, 10, 34, 38]. As illustrated in Figure 1.3, microfluidic technology shows superior controllability and great potential in the construction of these three kinds of functional materials, and

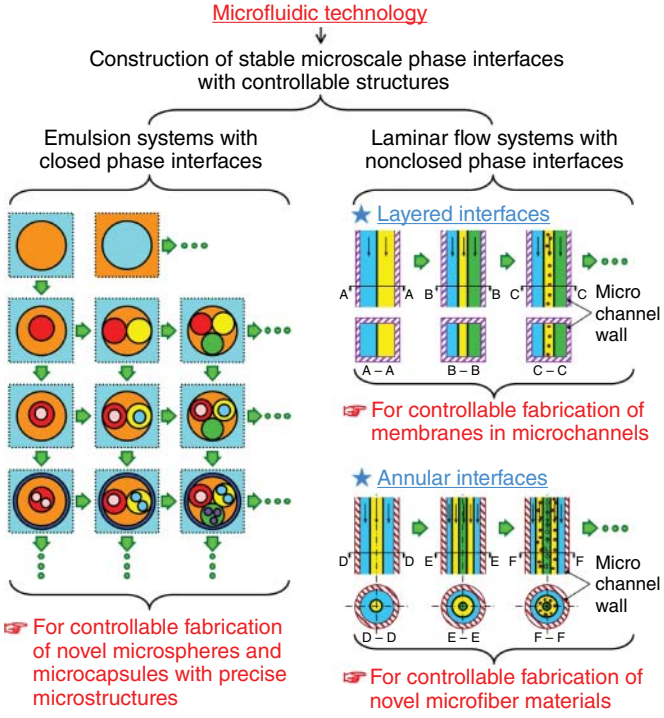

Figure 1.3 The system diagram of microfluidic method for the construction of stable microscale phase interfaces and for controllable preparation of novel functional materials.

can play its unique advantages in controllable construction of new functional materials with new structures, new functions, and high-performance features.

1.2 Microfluidic Fabrication of Microspheres and Microcapsules from Microscale Closed Liquid–Liquid Interfaces

Due to the small size and controllable internal structure, microspheres and microcapsules can be used as microcarriers, microreactors, microseparators, and microstructural units in drug delivery, substance encapsulation, chemical catalysis, biochemical separation, artificial cells, and enzyme immobilization, and have very broad application prospects. Microspheres and microcapsules are generally fabricated by using emulsion droplets with stable closed liquid–liquid interfaces (e.g., single water-in-oil (W/O) or oil-in-water (O/W) emulsions, W/O/W or O/W/O double emulsions, or even more complicated multiple emulsions) as templates, through subsequent polymerization, cross-linking, solvent evaporation, curing, and assembling in emulsion droplets or at interfaces. Traditional methods for the preparation of emulsion droplets are mainly achieved by mechanical stirring or fluid shear; thus, the sizes and the internal

structures of the droplets and the resultant template-fabricated microspheres and microcapsules are difficult to be controlled precisely, which greatly affect the performances and applications of the microspheres and microcapsules.

Microfluidic technology, which can generate emulsion droplets by emulsifying disperse phase to continuous phase through microchannels with co-flow, flow-focusing, or T-junction geometries, can achieve continuous and precise control of the microstructures of emulsion droplets, exhibiting significant superiority in the fabrication of microspheres and microcapsules with controllable size distributions and microstructures.

Researchers from all over the world have made a lot of important progress in the use of microfluidics to construct microscale closed liquid–liquid interfaces and then fabricate monodisperse microspheres and microcapsules [4, 5, 7–32]. In the preparations of microspheres and microcapsules with microfluidic approaches, most of them are focused on the use of microfluidic-generated W/O or O/W single emulsions (as shown in the first row in the upper left corner of Figure 1.3) as templates for preparing monodisperse microspheres, or the use of W/O/W or O/W/O double emulsions (as shown in the second row in the first column of the upper left corner of Figure 1.3) as templates for preparing monodisperse core–shell microcapsules. Some studies have also attempted to prepare some materials with new structures such as multicore microspheres, Janus microspheres, and nonspherical particles by microfluidic technology.

The authors' group controllably constructed multiple emulsion systems with complex microscale multiphase multicomponent liquid–liquid interfaces by building series and parallel microchannels [31]. These emulsions are used as templates for controllably preparing multiphase multicomponent microspheres and microcapsules for the encapsulation of substances [29], as well as new multifunctional microspheres and microcapsules with complex structures [28, 30].

1.3 Microfluidic Fabrication of Membranes in Microchannels from Microscale Nonclosed Layered Laminar Interfaces

Because of the excellent performances in catalysis, separations, purifications, analysis and detection, controlled release, emulsification, and so on, functional membrane materials are considered as one of the important supporting technologies for sustainable development. If the combination of membrane materials and microfluidic technology is obtained, it will play the synergy of the two to achieve the integration of functional materials and components. In this way, it can not only promote the application of membrane materials in microseparation and microanalysis but also provide new catalysis- or reaction-separation coupling technologies for microchemical or microreaction processes, showing very broad application prospects [6]. Therefore, as a new technology platform, membrane-in-microchannel technology is increasingly subject to different disciplines of international attention [6].

In a co-flow microchannel, when immiscible multiphase fluids flows into the same microchannel, stable layered laminar flow patterns can be formed through

microfluidic laminar flow technology [36] ("Layered interfaces" in Figure 1.3). In each phase, the fluid can maintain its flow pattern unchanged; chemical reactions such as polymerization and cross-linking only occur at the liquid–liquid interfaces, forming monolayer or multilayer parallel ultrathin membranes in the microchannels.

The microchannels can be divided into several independent channels by the membranes in microchannels. Due to the selective permeability or adsorption ability of functional membrane materials, selective separation, extraction, detection, and analysis can be realized with the membranes in the microchannels. Catalysts can also be effectively deposited on the membrane surfaces, thereby increasing the specific surface area of the catalytic material within a microchannel, to accelerate the rate of catalytic reaction in the microchannel. In addition, environmental stimuli-responsive smart membranes, which can regulate the effective membrane pore size and permeability in response to the change in physical or chemical signals in the environment, show incomparable superiority over traditional membranes [39]. If the smart membranes can be combined with microfluidics, it will undoubtedly provide efficient technology platform for the intensification of microseparation, microanalysis and detection, microreaction processed, and the enhancement of membrane performances.

Since the fabrication processes of membranes in microchannels are different from traditional membrane preparation processes, so far there are only a few reports on the fabrications of membranes with limited materials such as polyamide and chitosan in microchannels by using microfluidic laminar flow technology [6, 33, 36, 37, 40, 41].

1.4 Microfluidic Fabrication of Microfiber Materials from Microscale Nonclosed Annular Laminar Interfaces

Microfiber materials have a wide range of applications in optoelectronics, biomedicine, chemical industry, light industry, and other fields, wherein the hollow fiber membranes play an important role in the chemical separation processes. Currently, the preparations of microfiber materials are mainly achieved by using melt spinning method, electrospinning method, and other methods, while these methods are still difficult to achieve precise control of the microstructures of microfiber materials or impart multifunctional characteristics. Therefore, it is still necessary to seek new preparation processes and methods for the preparation of microfiber materials, and the microfluidic laminar flow technology is a very promising new method.

With microfluidic laminar flow technology, stable annular laminar flow patterns of immiscible multiphase fluids can be formed in the microchannels [4] ("Annular interfaces" in Figure 1.3). With these stable annular multiphase laminar interface systems as templates, microfiber materials including linear solid microfibers, hollow tubular microfibers, and core–shell composite microfibers can be fabricated by reaction or curing at the liquid–liquid interfaces or inside phases.

Since microfluidic technology enables continuous and accurate control over the annular liquid–liquid interfaces of laminar flows, it can provide optimal design of fibrous material synthesis systems. Therefore, compared with traditional spinning techniques, microfluidic technology has significant advantages in precise regulation and design of microfiber microstructures: it improves performances and imparts multifunctional characteristics of microfiber materials [4, 34, 36, 38, 42–47].

Microfluidic technology has been used to successfully prepare calcium alginate, polyvinyl alcohol, poly(lactic-*co*-glycolic acid), liposomes, chitosan, poly(ether sulfone), and polyacrylonitrile microfibers [34, 38, 42–47], which show excellent flexibility and extraordinary potential in the construction of microscale annular liquid–liquid interfaces and preparation of microfiber materials.

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2

Shear-Induced Generation of Controllable Multiple Emulsions in Microfluidic Devices

2.1 Introduction

Multiple emulsions are complex nested liquid systems, containing liquid droplets of decreasing sizes placed one inside another. They are widely used as encapsulation systems in myriad applications, including drug delivery [1–3], foods [4, 5], cosmetics [6, 7], chemical separations [8, 9], and as templates for syntheses of microspheres and microcapsules [10–16]. Accurate control of the size monodispersity and internal structure of multiple emulsions are critical for their versatility because these features enable precise manipulation of the loading levels and the release and transport kinetics of the encapsulated substances [10–21]. Although there have been several reports on the preparation of monodisperse multiple emulsions [13–23], accurate control of both the size and structure of the emulsions remains difficult to achieve, and current techniques are not scalable for fabricating higher order multiple emulsions.

Typically, multiple emulsions can be generated via sequential bulk emulsification using shear. This method usually produces emulsions with polydisperse size. Controlling the shear with constrained geometry [24–28], porous membranes [17, 21], or microchannels [18] can produce emulsions with nearly monodisperse size; these can then themselves be emulsified to produce multiple emulsions. However, although the volume fractions of both the initial and final emulsions can be manipulated [17, 18, 21, 24–27], accurate control over the number of inner droplets in multiple emulsions remains difficult by using these techniques. However, there are many cases where control of the inner droplet number is more important than control of their volume fraction. For example, with precise control of the number and size of inner droplets, transport kinetics of encapsulated substances in the emulsions can be precisely manipulated. Control of the inner droplet number is also critical for engineering colloidal assemblies to produce nonspherical particles [29]. Moreover, it is still challenging for co-encapsulation of droplets containing distinct contents in multiple emulsions, with accurate control of the number, ratio, and size of different inner droplets within each level. With such control on the structure of multicomponent multiple emulsions, these emulsions can offer advanced platforms for design of more complex multicompartment materials and provide synergistic delivery systems or chemical microreactors for incompatible actives or chemicals with versatile encapsulation and flexible mass-transfer kinetics.

Microfluidics for Advanced Functional Polymeric Materials, First Edition. Liang-Yin Chu and Wei Wang.

Microfluidic techniques provide an alternate route to generate monodisperse multiple emulsions. Cascading two T-junction geometries [19, 23] can generate monodisperse double emulsions with some control over the number and size of inner droplets. However, the microfluidic device with standard two-dimensional (2D) microchannels requires precise, localized modification of the microchannel wettability for producing multiple emulsions. This ultimately restricts their utility. By contrast, coaxial flow-focusing [13, 14, 16] geometries relax the constraints for wettability modification, but are still limited in the range of fluids that can be used and in the accurate control afforded over the number and size of inner droplets. Moreover, co-encapsulation of multicomponent droplets in multiple emulsions with precise control of their number, ratio, and size within each level, cannot be easily achieved with these devices. In addition, current microfluidic approaches cannot be scaled up for producing higher order multiple emulsions, such as triple emulsions.

The authors' group developed a highly scalable and versatile microfluidic strategy for controllable shear-induced generation of monodisperse multiple emulsions. In this chapter, the microfluidic devices for controllable emulsion generation and the controllable microfluidic fabrication of single emulsions, double emulsions, triple emulsions, and multicomponent multiple emulsions with even more complex structures are introduced.

2.2 Microfluidic Strategy for Shear-Induced Generation of Controllable Emulsion Droplets

Usually, microfluidic devices for generating emulsion droplets consist of droplet-making units and connecting units. The droplet-making units usually contain microchannels with co-flow (Figure 2.1a) [31], flow-focusing (Figure 2.1b) [32], and T-junction (Figure 2.1c) [19] geometries for generating emulsion droplets, while the connecting units usually contain microchannels for manipulating the generated droplets.

Typically, the microchannels in microfluidic device can be constructed by coaxially inserting cylinder glass capillaries into square glass tubes. The inner microchannel of the inserted capillary and the interstice space between the inserted capillary and square tube create three-dimensional (3D) microchannels for flowing different fluids. After fixing such assembly structures of glass capillaries and tubes on glass plates, microfluidic device with microchannels for emulsion generation can be fabricated [33, 34]. The glass-capillary microfluidic device can be used for emulsion generation without microchannel surface modification due to their 3D microchannel structure, but the fabrication process of these devices requires troublesome manual assembling. Alternatively, based on soft lithography, 2D microchannels can be etched on polydimethylsiloxane (PDMS) plates for fabrication of microfluidic devices [35]. These PDMS microfluidic devices allow flexible construction of microchannel networks for generation and manipulation of droplets. Meanwhile, their fabrication process based on the well-established soft lithography technique allows massive production of the devices. However, these PDMS devices require troublesome