Rheology of Viscoelastic Fluids in Microfluidic: From Theoretical Research to Practical Applications

Huan Wang

Department of Bioengineering, Qilu University of Technology (Shandong Academy of Sciences) Ji Nan, 250353 China

*Corresponding author e-mail: wh1221233@126.com

Abstract. Viscoelastic fluids exhibit unique flow behaviors due to their combined elastic and viscous properties, which significantly influence particle dynamics in microfluidic systems. This review summarizing the underlying mechanisms, influencing factors, and potential applications. Additionally, we explore the practical applications of viscoelastic fluid-induced particle migration in biomedical diagnostics, and chemical engineering. Future research directions are suggested to further enhance the understanding and utilization of viscoelastic fluid interface effects for advanced microfluidic technologies.

Keywords: Viscoelastic Fluids; Microfluidic, Practical Applications.

1. Introduction

Microfluidic technology has gained significant attention due to its higher surface-to-volume ratio, faster mass and heat transfer rates, and potential for precise control over fluid dynamics. It has found broad applications in biomedical analysis, chemical reaction control, and fluid physics research. Viscoelastic fluids are those containing polymers, suspended particles, or biological macromolecules. Many biological fluids (such as blood and extracellular matrix) exhibit inherent viscoelasticity. By introducing macromolecules into solvents to impart viscoelasticity, these fluids can be used to model the rheological properties of biological fluids. They exhibit unique nonlinear flow characteristics in microfluidic systems, such as shear thinning or shear thickening behaviors. The rheological properties of viscoelastic fluids result in non-Newtonian fluid behavior at the microscale, which is crucial for the design and optimization of microfluidic systems This approach aids in studying biological processes and disease mechanisms under in vitro conditions and holds significant relevance in biomedical and chemical reaction engineering[1,2]The manipulation of viscoelastic fluids has been a major research focus, primarily investigating the rheological properties of the fluid, particle manipulation within the fluid, improvements in mixing efficiency, and the development of novel microfluidic devices [3].

This paper reviews the research progress and applications of viscoelastic fluids in microfluidic systems, focusing on the behavior of these fluids in microfluidic chips, focusing mechanisms, and particle manipulation. By referencing relevant literature, this paper aims to provide readers with a comprehensive overview of the current research on viscoelastic fluids in the field of microfluidics and to offer suggestions for future research directions. Future research needs to explore theoretical models, experimental systems, and clinical applications in depth, in order to fully realize the potential of microfluidic technology.

2. Principles

2.1 Migration Dynamics

In microchannels, viscoelastic fluids are typically influenced by inertial forces, elastic lift, and viscous forces. The relationships between these forces are described using dimensionless parameters: the Reynolds number, which is the ratio of inertial forces to viscous forces [4], characterizes the relative importance of these forces in fluid flow. The Weissenberg number (Wi) is used to compare the viscous forces with elastic forces [5]. The elasticity number characterizes the strength of elastic effects in polymer solutions during microscale flow. In spiral channels, the Dean number is also involved [6], which directly represents the ratio of centrifugal forces to viscous forces, and also measures the intensity of secondary flows. In viscoelastic fluids, the normal stress difference is an important concept, describing the stress differences in different directions during fluid flow. This stress difference is usually related to the elastic behavior of the fluid and plays a critical role in the fluid's flow characteristics. The normal stress difference typically refers to the first normal stress difference (N_1) and the second normal stress difference (N_2). Normal stress differences are influenced by various factors, including the fluid's elasticity, molecular structure, shear rate, and the interaction between the fluid and the flow channel. In microfluidic channels, due to their small dimensions, these effects may become more pronounced. Experimental studies and theoretical analyses have shown that the normal stress difference can lead to various flow phenomena, such as die swell and the Weissenberg rod-climbing effect. These phenomena have significant industrial applications, such as in polymer processing and food processing. Numerical simulations are an effective method for studying the normal stress differences in the flow of viscoelastic fluids. Alves et al. discussed in detail the application of numerical methods in simulating the flow of viscoelastic fluids, providing a theoretical foundation for the prediction and control of fluid morphology in microfluidics [7]. Furthermore, viscoelastic fluids are also used in fields such as cell sorting, rare cell detection, and imaging flow cytometry [8,9].

2.2 Mixing Dynamics

In the field of microfluidics, the study of mixing mechanisms is often mentioned. Mixing methods typically rely on the generation of chaotic advection and/or turbulence, where fluid motion is irregular, leading to random variations in pressure and velocity over both space and time. Chaotic advection can be generated by stirring the flow, and it is particularly effective at low Reynolds numbers, as the resulting species flow undergoes splitting, stretching, folding, and breakdown. Traditional mixing methods rely on molecular diffusion, which is inefficient at the microscale due to the typically laminar flow in microchannels. Mixing occurs solely due to molecular diffusion between layers with different concentrations. Therefore, when the thickness of each fluid layer exceeds the characteristic diffusion length (typically around Dt where it is the residence time of the substance), achieving efficient and rapid mixing is extremely difficult. However, the introduction of viscoelastic fluids provides new possibilities for microfluidic mixing. Viscoelastic fluids achieve efficient mixing in microfluidic through three synergistic mechanisms: Elastic instability-induced flow bifurcation occurs when the Deborah number (De) exceeds a critical threshold (De_{crit}≈0.316), generating bistable reversed flow that stretches and folds interfaces, as demonstrated in UCM fluid within mixing-separating cells .(2)Normal stress-driven chaotic advection creates asymmetric vortices in contraction-expansion geometries[10], reorganizing fluid layers through viscoelastic effects [11].(3)Synergy with Dean vorticesinduces secondary flows in curved channels to continuously stretch/fold interfaces[12], boosting mixing efficiency above 90%.These mechanisms enable millisecond-scale mixing (e.g., 88.2% efficiency in 4.1 ms using sharp-corner designs)[13], ideal for sensitive biological samples.

3. Applications

3.1 Manipulation of biological particles

Biological micro/nanoparticles, including cells, platelets, bacteria, and extracellular vesicles, are typically suspended in biological fluids (e.g., blood) exhibiting non-Newtonian fluid characteristics [14]. Precise manipulation of these particles within microfluidic technologies is crucial for applications like cell analysis, infectious disease detection, and tumor diagnosis. Leveraging the properties of non-Newtonian fluids enables size-based, label-free separation of particles and cells. This technology holds significant potential for enhancing the sensitivity and accuracy of blood sample processing [15].

Furthermore, simulating hemodynamics in blood vessels facilitates more accurate prediction and control of blood-vessel wall interactions, which is crucial for cardiovascular disease research [16].

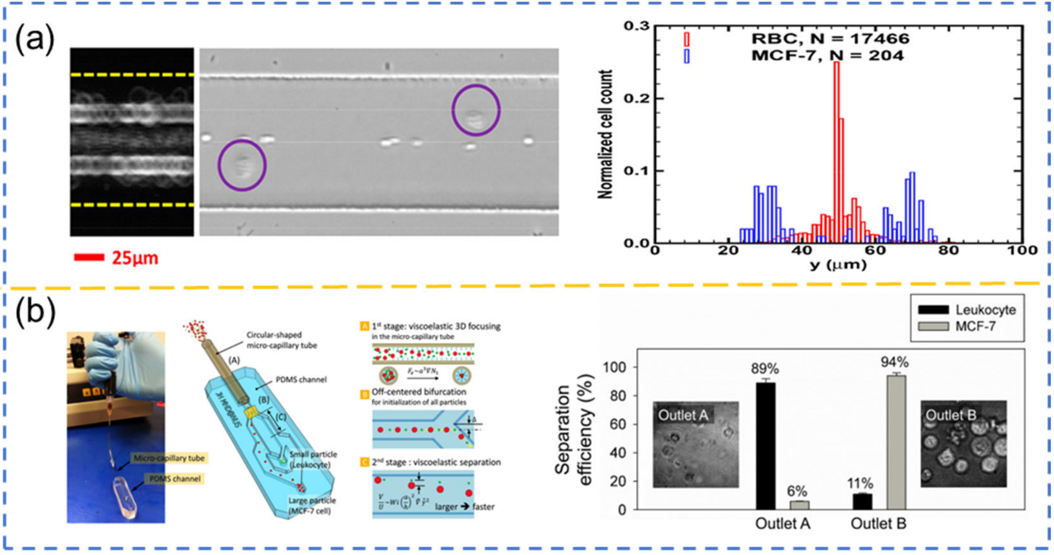

Figure1 (a) The separation of Michigan Cancer Foundation-7 (MCF-7)and The normalized cell count plot is shown for the separation of MCF-7 cells and RBCs[17] (b) The hybrid capillary-inserted microfluidic device and MCF-7 cell separation from white blood cells (WBCs) [18]

Viscoelastic microfluidic technology leverages the physical properties of biological particles (e.g., size, deformability, and rheological responses) to demonstrate unique advantages in label-free manipulation and sorting. To address the heterogeneity of biological samples, its applications can be categorized into two primary directions based on the size gradient of target particles. First-level sorting focuses on large-sized tumor cells (15-30 μm). When cell diameter exceeds the critical threshold of 15 μm, the normal stress difference (N1) generated by the viscoelastic core flow within the microchannel dominates the migration process. Elastic lift forces drive tumor cells toward the flow field center, while inertial effects on smaller particles are suppressed, enabling efficient spatial separation.

Lu and Xuan explored the continuous particle separation technique (eiPFF) based on elastic and inertial lift in viscoelastic solutions. They systematically studied the parameter effects in eiPFF and found that it provided higher particle throughput and separation resolution compared to traditional space-effect-based PFF. Particularly, when the Reynolds number (Re) is around 1, the efficiency of eiPFF is maximized, filling the gap in iPFF technology at Re numbers of 10 or higher. [17,19] , as shown in Figure1(a).Jeonghun Nam developed a two-stage microfluidic device based on viscoelastic fluids that achieves efficient sorting of tumor cells through a size-dependent lateral migration mechanism. This device first performs three-dimensional pre-alignment of particles (including MCF-7 cells) and then completes separation in the expansion region. At a flow rate of 200 μl/min, it attains a 94% separation efficiency for MCF-7 cells with a purity of approximately 97%, while maintaining ~90% cell viability (via trypan blue exclusion assay), demonstrating its high adaptability and effectiveness in tumor cell sorting. [18], .as shown in Figure1(b).

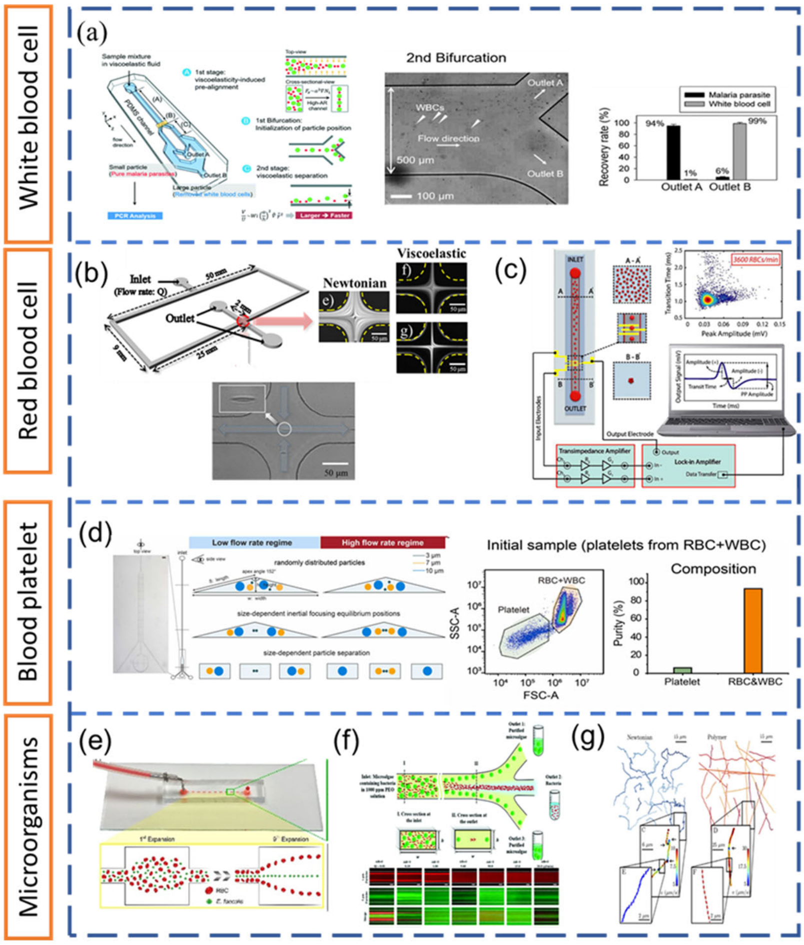

Figure2.(a) A device for the concentration and cleaning of white blood cells (WBCs) using viscoelastic fluids.[20](b) Typical image of a stretched RBC at a flow rate of 160 µ L/h[21] (c) Illustration of the impedance-based viscoelastic flow cytometer[22] (d) Separation of platelets, red blood cells, and white blood cells based on size using a microfluidic triangular channel (0.3% w/v PEO)[23] (e) Schematic diagram of particle migration and separation of red blood cells and bacteria in a cascaded contraction-expansion microchannel.[24](f) Microalgal Chlorella samples separation of Bacillus subtilis bacteria.[25](g) Dynamics of bacteria under viscoelastic flow. Cell tumbling decreases, velocity increases, leading to enhanced translational diffusion and a sharp reduction in rotational diffusion.[26]

Second-level sorting targets small-to-medium-sized biological particles (≤ 15 µm), including blood cell subpopulations and microbes. Due to their size being comparable to the characteristic scale of the flow field, their trajectories are governed by the nonlinear coupling of inertial and viscoelastic effects. For >10 µm cells, Nam et al. [20,27] developed high-aspect-ratio devices for efficient leukocyte-parasite separation (near-complete removal) and 18× leukocyte enrichment, even in viscous blood.as shown in Figure(a). Kim et al.[28–30] integrated piezoelectric pumps for throughput/concentration, overcoming purity limitations in inertial microfluidics. Intermediate-sized RBCs serve as rheological models for disease biomarker detection. Parameters such as polymer concentration and flow velocity gradients can be optimized to achieve secondary precision screening (e.g., distinguishing white blood cells from red blood cells as shown in Figure(b c), or isolating bacteria .as shown in Figure(f)).For platelets (2–4 µm), Nam et al. designed sheathless PDMP isolation from blood [31,32] Bacterial separation achieved >98% efficiency in cascaded channels (Bilican [24,31,32]), as shown in Figure(e). Viscoelastic microfluidics enables size-based particle manipulation across scales:76% whole-blood capture (Faridi et al. [33]), and ±1 µm precision focusing (Holzner et al. [8]). Rheology studies reveal polymer-enhanced linear swimming [26], .as shown in Figure(g). shear stress effects via "strangulation number"[34], and adhesion suppression via elastic lift [35].For <1 µm particles, Jeon et al. [36] optimized dimensionless parameters for precise platelet/E. coliseparation and nanoparticle removal. Integration of flow parameters and mechanical mechanisms enables full-scale sorting from mm to nm. Innovations include asymmetric sheath flow

(62% recovery, Wu et al.[37], viscoelastic/Newtonian co-flow (Tian et al. [38]), shape-based sorting (Liu et al. [39,40]), and two-step Candidaconcentration (74.6×, Lim et al. [41]). These synergize optimized parameters with rheological mechanisms for efficient microbial separation and detection.

3.2 Mixing

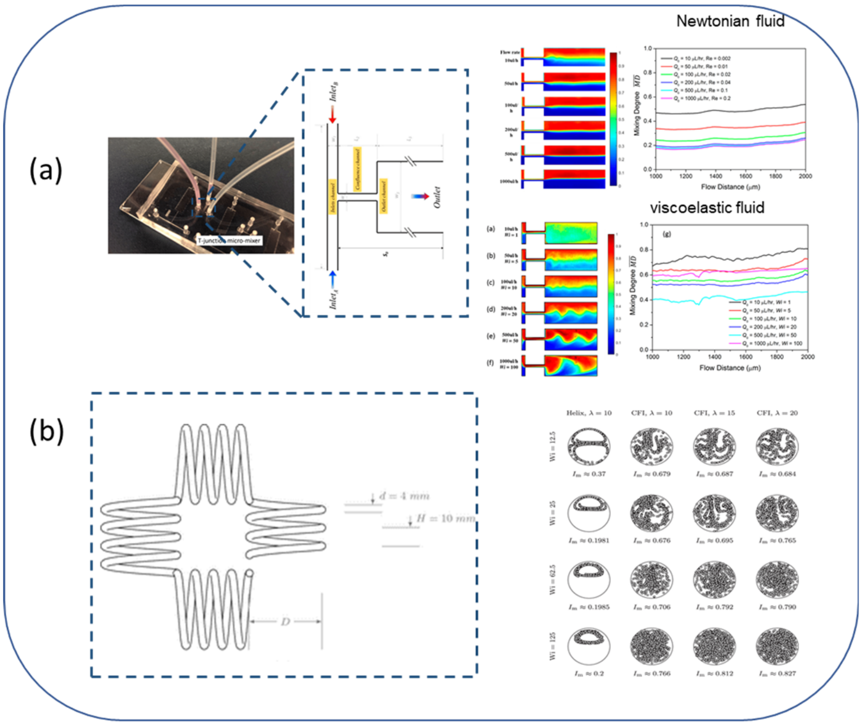

Figure3 (a) Concentration profile of viscoelastic fluid and Newtonian fluid at different constant flow rates.[42]. (b) Sketch of the CFI geometry[43]

Viscoelastic mixing leverages rheological properties and channel geometries for efficient low-Re mixing. Passive designs achieve >80% efficiency: Zhang et al. [42] used T-mixer elastic vortices (mixing degree 0.82), as shown in Figure 4(a).Fan et al. [13] employed sharp-corner stretching/folding (88.2% efficiency), and spiral mixers harness Dean vortices with flow-rate-dependent enhancement (Verma et al. [43]. as shown in Figure 4(b). Cochraneet al. [44] analyzed geometry-rheology coupling.

Novel instabilities optimize mixing: Gan et al. [45] triggered "whipping" flow via contraction/expansion, while Samanta et al. [46] proposed elastic-inertial turbulence (EIT) theory showing elastic-dominated chaos suppresses Newtonian turbulence. Rheological studies reveal nonmonotonic reverse flow (Afonso et al. [47]), polymer-dependent instability modulation (Wu et al. [48]), and elastic wave energy transfer (Li et al. [49]).

References

[1] Yang S, Kim J Y, Lee S J, et al. Sheathless elasto-inertial particle focusing and continuous separation in a straight rectangular microchannel[J]. Lab on a Chip, 2011, 11(2): 266-273.

[2] Huang P Y, Joseph D D. Effects of shear thinning on migration of neutrally buoyant particles in pressure driven flow of Newtonian and viscoelastic fluids[J]. Journal of Non-Newtonian Fluid Mechanics, 2000, 90(2): 159-185.

[3] D'Avino G, Romeo G, Villone M M, et al. Single line particle focusing induced by viscoelasticity of the suspending liquid: theory, experiments and simulations to design a micropipe flow-focuser[J]. Lab on a Chip, 2012, 12(9): 1638-1645.

[4] Rott N. Note on the History of the Reynolds Number[J]. Annual Review of Fluid Mechanics, 1990, 22(Volume 22, 1990): 1-12.

[5] Thompson R L, Oishi C M. Reynolds and Weissenberg numbers in viscoelastic flows[J]. Journal of Non-Newtonian Fluid Mechanics, 2021, 292: 104550.

[6] Liu C, Ding B, Xue C, et al. Sheathless Focusing and Separation of Diverse Nanoparticles in Viscoelastic Solutions with Minimized Shear Thinning[J]. Analytical Chemistry, 2016, 88(24): 12547-12553.

[7] Alves M A, Oliveira P J, Pinho F T. Numerical Methods for Viscoelastic Fluid Flows[J]. Annual Review of Fluid Mechanics, 2021, 53(1): 509-541.

[8] Holzner G, Stavrakis S, deMello A. Elasto-Inertial Focusing of Mammalian Cells and Bacteria Using Low Molecular, Low Viscosity PEO Solutions[J]. Analytical Chemistry, 2017, 89(21): 11653-11663.

[9] Di Carlo Dino, Irimia Daniel, Tompkins Ronald·, et al. Continuous inertial focusing, ordering, and separation of particles in microchannels[J]. Proceedings of the National Academy of Sciences, 2007, 104(48): 18892-18897.

[10] Lee C Y, Wang W T, Liu C C, et al. Passive mixers in microfluidic systems: A review[J]. Chemical Engineering Journal, 2016, 288: 146-160.

[11] Julius L A N, Jagannadh V K, Michael I J, et al. Design and validation of on-chip planar mixer based on advection and viscoelastic effects[J]. BioChip Journal, 2016, 10(1): 16-24.

[12] Sudarsan A P, Ugaz V M. Multivortex micromixing[J]. Proceedings of the National Academy of Sciences, 2006, 103(19): 7228-7233.

[13] Fan L L, Zhu X L, Zhao H, et al. Rapid microfluidic mixer utilizing sharp corner structures[J]. Microfluidics and Nanofluidics, 2017, 21(3): 36.

[14] Tian F, Feng Q, Chen Q, et al. Manipulation of bio-micro/nanoparticles in non-Newtonian microflows[J]. Microfluidics and Nanofluidics, 2019, 23(5): 68.

[15] Tang D, Jiang L, Tang W, et al. Cost-effective portable microfluidic impedance cytometer for broadband impedance cell analysis based on viscoelastic focusing[J]. Talanta, 2022, 242: 123274.

[16] Pinching threads, singularities and the number 0.0304... | Physics of Fluids | AIP Publishing[EB/OL]. (1996)[2024-10-05]. https://pubs.aip.org/aip/pof/article-abstract/8/11/2827/260014/Pinching-threads-singularities-and-the-number-0?redirectedFrom=fulltext.

[17] Liu C, Xue C, Chen X, et al. Size-Based Separation of Particles and Cells Utilizing Viscoelastic Effects in Straight Microchannels[J]. Analytical Chemistry, 2015, 87(12): 6041-6048.

[18] Nam J, Tan J K S, Khoo B L, et al. Hybrid capillary-inserted microfluidic device for sheathless particle focusing and separation in viscoelastic flow[J]. Biomicrofluidics, 2015, 9(6): 064117.

[19] Lu X, Xuan X. Inertia-Enhanced Pinched Flow Fractionation[J]. Analytical Chemistry, 2015, 87(8): 4560-4565.

[20] Nam J, Shin Y, Tan J K S, et al. High-throughput malaria parasite separation using a viscoelastic fluid for ultrasensitive PCR detection[J]. Lab on a Chip, 2016, 16(11): 2086-2092.

[21] Cha S, Shin T, Lee S S, et al. Cell Stretching Measurement Utilizing Viscoelastic Particle Focusing[J]. Analytical Chemistry, 2012, 84(23): 10471-10477.

[22] Serhatlioglu M, Asghari M, Tahsin Guler M, et al. Impedance-based viscoelastic flow cytometry[J]. ELECTROPHORESIS, 2019, 40(6): 906-913.

[23] Cho E, Kim J ah, Aslan M K, et al. Tunable viscoelastic size-based particle separation in straight microchannels with triangular cross-sections[J]. Sensors and Actuators B: Chemical, 2024, 414: 135892.

[24] Bilican I. Cascaded contraction-expansion channels for bacteria separation from RBCs using viscoelastic microfluidics[J]. Journal of Chromatography A, 2021, 1652: 462366.

[25] Yuan D, Zhao Q, Yan S, et al. Sheathless separation of microalgae from bacteria using a simple straight channel based on viscoelastic microfluidics[J]. Lab on a Chip, 2019, 19(17): 2811-2821.

[26] Patteson A E, Gopinath A, Goulian M, et al. Running and tumbling with E. coli in polymeric solutions[J]. Scientific Reports, 2015, 5: 15761.

[27] Nam J, Jang W S, Lim C S. Non-electrical powered continuous cell concentration for enumeration of residual white blood cells in WBC-depleted blood using a viscoelastic fluid[J]. Talanta, 2019, 197: 12-19.

[28] Gou Y, Zhang S, Sun C, et al. Sheathless Inertial Focusing Chip Combining a Spiral Channel with Periodic Expansion Structures for Efficient and Stable Particle Sorting[J]. Analytical Chemistry, 2020, 92(2): 1833-1841.

[29] Kim J, Lim H, Jee H, et al. High-Throughput Cell Concentration Using A Piezoelectric Pump in Closed-Loop Viscoelastic Microfluidics[J]. Micromachines, 2021, 12(6): 677.

[30] Xiang N, Shi X, Han Y, et al. Inertial Microfluidic Syringe Cell Concentrator[J]. Analytical Chemistry, 2018, 90(15): 9515-9522.

[31] Nam J, Yoon J, Jee H, et al. High-Throughput Separation of Microvesicles from Whole Blood Components Using Viscoelastic Fluid[J]. Advanced Materials Technologies, 2020, 5(12): 2000612.

[32] Nam J, Lim H, Kim D, et al. Continuous separation of microparticles in a microfluidic channel via the elasto-inertial effect of non-Newtonian fluid[J]. Lab on a Chip, 2012, 12(7): 1347-1354.

[33] Faridi M A, Ramachandraiah H, Banerjee I, et al. Elasto-inertial microfluidics for bacteria separation from whole blood for sepsis diagnostics[J]. Journal of Nanobiotechnology, 2017, 15(1): 3.

[34] Qu Z. Effects of shear-thinning viscosity and viscoelastic stresses on flagellated bacteria motility[J]. Physical Review Fluids, 2020, 5(7).

[35] Cao Ding, Dvoriashyna M, Liu Song, et al. Reduced surface accumulation of swimming bacteria in viscoelastic polymer fluids[J]. Proceedings of the National Academy of Sciences, 2022, 119(45): e2212078119.

[36] Jeon H, Lee S H, Shin J, et al. Elasto-inertial microfluidic separation of microspheres with submicron resolution at high-throughput[J]. Microsystems & Nanoengineering, 2024, 10(1): 1-14.

[37] Wu Z, Willing B, Bjerketorp J, et al. Soft inertial microfluidics for high throughput separation of bacteria from human blood cells[J]. Lab on a Chip, 2009, 9(9): 1193-1199.

[38] Tian F, Zhang W, Cai L, et al. Microfluidic co-flow of Newtonian and viscoelastic fluids for high-resolution separation of microparticles[J]. Lab on a Chip, 2017, 17(18): 3078-3085.

[39] Liu P, Liu H, Semenec L, et al. Length-based separation of Bacillus subtilis bacterial populations by viscoelastic microfluidics[J]. Microsystems & Nanoengineering, 2022, 8(1): 1-11.

[40] Liu P, Liu H, Yuan D, et al. Separation and Enrichment of Yeast Saccharomyces cerevisiae by Shape Using Viscoelastic Microfluidics[J]. Analytical Chemistry, 2021, 93(3): 1586-1595.

[41] Lim H, Kim J Y, Choo S, et al. Separation and Washing of Candida Cells from White Blood Cells Using Viscoelastic Microfluidics[J]. Micromachines, 2023, 14(4): 712.

[42] Zhang M, Zhang W, Wu Z, et al. Comparison of Micro-Mixing in Time Pulsed Newtonian Fluid and Viscoelastic Fluid[J]. Micromachines, 2019, 10(4): 262.

[43] Verma V, Topalović A, Monechi G, et al. Mixing of Viscoelastic Fluid Flows in a Coiled Flow Inverter[J]. Industrial & Engineering Chemistry Research, 2020, 59(9): 3854-3864.

[44] Cochrane T, Walters K, Webster M F. On Newtonian and Non-Newtonian Flow in Complex Geometries[J]. Philosophical Transactions of the Royal Society of London. Series A, Mathematical and Physical Sciences, 1981, 301(1460): 163-181.

[45] Gan H Y, Lam Y C, Nguyen N T, et al. Efficient mixing of viscoelastic fluids in a microchannel at low Reynolds number[J]. Microfluidics and Nanofluidics, 2007, 3(1): 101-108.

[46] Samanta D, Dubief Y, Holzner M, et al. Elasto-inertial turbulence[J]. Proceedings of the National Academy of Sciences, 2013, 110(26): 10557-10562.

[47] Afonso A M, Alves M A, Poole R J, et al. Viscoelastic flows in mixing-separating cells[J]. Journal of Engineering Mathematics, 2011, 71(1): 3-13.

[48] Wu S, Raihan M K, Song L, et al. Polymer effects on viscoelastic fluid flows in a planar constriction microchannel[J]. Journal of Non-Newtonian Fluid Mechanics, 2021, 290: 104508.

[49] Li Yuke, Steinberg Victor. Mechanism of vorticity amplification by elastic waves in a viscoelastic channel flow[J]. Proceedings of the National Academy of Sciences, 2023, 120(28): e2305595120.