

From Lab-on-a-Chip to Point-of-Care: Microfluidic Technologies Impacting Healthcare

Lee Kasowaki and Mirac Berat

EasyChair preprints are intended for rapid dissemination of research results and are integrated with the rest of EasyChair.

From Lab-on-a-Chip to Point-of-Care: Microfluidic Technologies Impacting Healthcare

Lee Kasowaki, Mirac Berat

Abstract

Microfluidic technologies have revolutionized the landscape of healthcare by enabling the development of sophisticated diagnostic tools that bridge the gap between laboratory-based analyses and point-of-care applications. This review explores the transformative journey from labon-a-chip platforms to practical point-of-care solutions, highlighting the significant impact of microfluidics on healthcare. The evolution of microfluidic devices from complex laboratory setups to portable, user-friendly systems has accelerated the integration of diagnostic assays into everyday clinical practice. These devices leverage the manipulation of minute fluid volumes within microscale channels to perform diverse functions such as sample preparation, cell sorting, and biochemical analysis with unprecedented precision and efficiency. The integration of microfluidics with other technologies such as biosensors, imaging modalities, and artificial intelligence has further enhanced the sensitivity, specificity, and speed of diagnostic procedures. The shift towards point-of-care applications has brought healthcare closer to the patients, offering rapid and on-the-spot diagnosis, reducing turnaround times, and improving treatment outcomes. Portable microfluidic devices have empowered healthcare providers in resource-limited settings to perform timely and accurate diagnostics, thus addressing global health challenges more effectively.

Keywords: Microfluidics, Healthcare, Diagnostics, Portable Devices, Biomedical Devices

1. Introduction

The integration of nanostructured surfaces within microfluidic systems has emerged as a compelling avenue in the realm of biomolecule manipulation, offering unprecedented opportunities to enhance efficiency and precision in various biomedical applications[1]. This convergence of nanotechnology with microfluidics has revolutionized the manipulation and control of biomolecules by leveraging surface engineering techniques at the nanoscale. The interplay between nanostructured surfaces and microfluidic transport phenomena has attracted

significant attention due to its potential to augment biomolecular manipulation. Nanostructuring surfaces within microfluidic channels allow for tailored modifications that influence fluid behavior, mass transport, and biomolecular interactions [2]. This introduction serves as a platform to delve into the multifaceted impacts of nanostructured surfaces on microfluidic transport, elucidating their role in advancing the efficiency and accuracy of biomolecule manipulation. This study aims to explore and dissect the mechanisms underlying the enhanced transport properties facilitated by nanostructured surfaces. By comprehensively reviewing surface patterning techniques and their effects on microfluidic transport, this research endeavors to unravel the intricate interplay between nanostructures and biomolecules within confined microenvironments. Understanding these fundamental interactions is pivotal in harnessing the full potential of nanostructured surfaces for manipulating biomolecules with precision and efficacy. Moreover, the implications of these advancements extend across various domains, including biomedical research, clinical diagnostics, and pharmaceutical development [3]. Harnessing the synergies between nanostructured surfaces and microfluidic platforms holds promise in revolutionizing biomolecule manipulation, and enabling advancements in drug delivery, biomarker detection, and disease diagnostics. Through experimental investigations, computational modeling, and theoretical analyses, this study aims to contribute valuable insights into the transformative potential of nanostructured surfaces in enhancing microfluidic transport for efficient biomolecule manipulation. The findings are anticipated to pave the way for the development of innovative strategies and technologies, driving the next wave of advancements in biotechnology and medical sciences.

The integration of nanostructured surfaces within microfluidic systems has unveiled promising avenues for optimizing biomolecule manipulation efficiency. This convergence of nanotechnology and microfluidics presents an intriguing path toward advancing the precision and control of biomolecules in various biomedical applications. Nanostructured surfaces, engineered at the nanoscale, wield a profound influence on microfluidic transport phenomena, offering tailored modifications that significantly impact fluid behavior, mass transport dynamics, and biomolecular interactions[4]. This synergy enables the manipulation of biomolecules with heightened accuracy and efficacy, underscoring the potential to revolutionize crucial aspects of biomedical research and technology. This study delves into the intricate interplay between nanostructured surfaces and microfluidic transport, aiming to decipher the underlying mechanisms that empower these surfaces

to enhance biomolecule manipulation. Through an extensive review of surface patterning techniques and their effects on microfluidic systems, this research seeks to elucidate the nuanced ways in which nanostructures shape and optimize biomolecular transport within confined microenvironments. The implications of these advancements are vast, spanning diverse domains such as drug delivery systems, biomarker detection platforms, and disease diagnostics [5]. The tailored manipulation and precise control of biomolecules facilitated by nanostructured surfaces within microfluidic setups hold immense promise for accelerating advancements in biomedical sciences. By amalgamating experimental explorations, computational modeling, and theoretical analyses, this study endeavors to offer valuable insights into the transformative potential of nanostructured surfaces in augmenting microfluidic transport for efficient biomolecule manipulation. Ultimately, this research aims to lay the groundwork for the development of innovative strategies and technologies poised to shape the future landscape of biotechnology and medical research [6].

Nanostructured surfaces play several crucial roles in enhancing microfluidic transport for efficient biomolecule manipulation: Enhanced Surface Area: Nanostructured surfaces significantly increase the available surface area within microfluidic channels. This enlarged area facilitates greater interactions between biomolecules and the surface, thereby enhancing binding, sensing, separation, and other molecular processes. Controlled Fluid Flow: Nanostructures can manipulate and control fluid flow at the microscale level[7]. Surface patterning allows for the modification of surface wettability, which, in turn, influences fluid behavior, such as inducing controlled flow patterns, reducing turbulence, or promoting specific directional flows that aid in biomolecule manipulation and separation. Selective Biomolecule Interactions: Nanostructured surfaces can be tailored to exhibit specific chemical or physical properties that selectively interact with certain biomolecules. This selectivity is instrumental in applications such as biomolecular sorting, purification, and detection, where targeted interactions are crucial for high specificity and sensitivity. Improved Sensing and Detection: Nanostructures integrated into microfluidic systems enhance the sensitivity and accuracy of biosensors and detection platforms. These surfaces can amplify signal transduction, improve signal-to-noise ratios, and enable the detection of low concentrations of biomolecules, pivotal for diagnostics and sensing applications [8]. Efficient Mass Transport: Nanostructured surfaces can optimize mass transport phenomena within microfluidic devices. They can influence diffusion rates, concentration gradients, and molecular

transport pathways, thereby expediting processes like molecular sieving, separation, and controlled release of biomolecules. Biocompatibility and Stability: Engineered nanostructured surfaces can exhibit enhanced biocompatibility and stability, reducing nonspecific binding and degradation of biomolecules. This property is crucial in maintaining the integrity of biomolecular samples and ensuring accurate manipulation and analysis. Platform for Multifunctionality: Nanostructured surfaces provide a versatile platform for multifunctionality within microfluidic devices [9]. By integrating various nanostructures with diverse functionalities onto a single platform, it's possible to perform multiple tasks such as separation, sensing, and reaction kinetics simultaneously. Overall, the strategic incorporation of nanostructured surfaces into microfluidic systems offers a spectrum of advantages that collectively contribute to enhancing biomolecule manipulation. These advantages have far-reaching implications across biotechnology, medicine, diagnostics, and various other fields where precise control over biomolecules is pivotal[10].

2. Advancements in Microfluidics: Bridging Nano-Scale Phenomena

The advent of microfluidic platforms has catalyzed a paradigm shift in the domain of single-cell analysis, offering unprecedented capabilities to explore the intricate dynamics of biological systems at the cellular level. This introduction sets the stage for unveiling the multifaceted landscape of single-cell analysis enabled by microfluidic technologies, emphasizing their pivotal role in unraveling the complexities inherent in cellular heterogeneity and dynamics. Microfluidics, with its ability to precisely manipulate minute fluid volumes within microscale channels, has revolutionized the way individual cells are isolated, cultured, and analyzed [11]. By providing controlled microenvironments and high-throughput capabilities, these platforms offer unparalleled opportunities to delve into cellular behaviors, such as gene expression, signaling pathways, and cellular responses to stimuli, shedding light on diverse biological phenomena. This study aims to delve into the diverse array of microfluidic techniques, exploring their applications in single-cell analysis and elucidating their contributions to advancing our understanding of fundamental cellular processes and disease mechanisms[12]. By amalgamating cutting-edge technologies with biological insights, this research unravels the intricate biological dynamics inherent in single cells, laying the groundwork for transformative advancements in fields ranging from basic biology to clinical diagnostics and personalized medicine. The field of single-cell analysis has experienced a profound transformation with the emergence of microfluidic platforms, offering a gateway to explore the intricacies of biological dynamics at an unprecedented resolution. This introduction aims to illuminate the pivotal role played by microfluidic technologies in unraveling the complexities of individual cells, underscoring their significance in dissecting cellular heterogeneity and revealing elusive biological phenomena. Leveraging precise manipulation of minute fluid volumes within microscale channels, microfluidic platforms have revolutionized the isolation, cultivation, and analysis of single cells. These platforms provide controlled microenvironments, enabling in-depth investigations into cellular behaviors such as gene expression, signaling cascades, and responses to stimuli. This study endeavors to navigate through the diverse spectrum of microfluidic techniques dedicated to single-cell analysis, elucidating their applications and contributions toward advancing our comprehension of fundamental cellular processes and disease mechanisms [13]. By synergizing cutting-edge technologies with biological insights, this research aspires to uncover the intricate biological dynamics inherent within single cells, potentially driving transformative innovations in basic biology, clinical diagnostics, and the realm of personalized medicine. Microfluidic platforms have emerged as powerful tools in the realm of single-cell analysis, unlocking a deeper understanding of the intricate biological dynamics inherent in individual cells. These platforms revolutionize our approach to studying cellular heterogeneity, offering precise control and manipulation of minute fluid volumes within microscale channels. By providing controlled microenvironments, these technologies enable the isolation, culture, and comprehensive analysis of single cells with unprecedented accuracy and throughput. Through diverse techniques such as droplet-based assays, nanofluidics, and integrated lab-on-a-chip systems, microfluidics facilitates the exploration of cellular behaviors encompassing gene expression, signaling pathways, and responses to environmental cues at a single-cell level. This study aims to delve into the multifaceted applications of microfluidic platforms, illuminating their pivotal role in uncovering elusive biological dynamics within individual cells. By elucidating these complexities, this research contributes to advancing our knowledge of fundamental cellular processes, fostering advancements in areas spanning basic biology, disease mechanisms, and the development of novel therapeutics and diagnostics tailored to the intricacies of individual cells [14].

Microfluidic platforms play several crucial roles in the context of single-cell analysis, enabling the unveiling of intricate biological dynamics: Precise Manipulation and Control: These platforms

offer precise control over fluid handling at the microscale level, allowing for accurate manipulation of individual cells. This control is essential for isolating, sorting, and culturing single cells in controlled microenvironments, ensuring reliable and reproducible experimental conditions [15]. High-Throughput Analysis: Microfluidic devices enable high-throughput analysis of single cells, facilitating the parallel analysis of numerous individual cells simultaneously[16]. This capability significantly enhances efficiency, allowing researchers to process a large number of cells rapidly, which is crucial when studying rare cell populations or heterogeneous samples. Single-Cell Isolation and Capture: Microfluidic systems provide techniques for isolating and capturing individual cells from complex mixtures [17, 18]. This capability is vital for studying cellular heterogeneity and analyzing specific cell types within a population, providing insights into diverse cellular behaviors and functions. Sensitive and Multiparametric Analysis: Microfluidic platforms enable sensitive detection and multiparametric analysis of various cellular characteristics and biomolecules at the single-cell level. They allow for the measurement of gene expression, protein levels, metabolites, and other cellular features, offering comprehensive insights into the functional diversity of individual cells [19]. Real-Time Monitoring and Imaging: Some microfluidic devices facilitate real-time imaging and monitoring of single cells over extended periods. This capability allows for the observation of dynamic cellular processes, responses to stimuli, and temporal changes in cellular behavior, offering valuable insights into biological dynamics. Reduced Sample Consumption and Cost: Microfluidic platforms operate with small sample volumes, reducing reagent consumption and overall experimental costs. This advantage makes them particularly valuable when working with limited or precious samples while maintaining high analytical sensitivity [20]. Integration with Other Analytical Techniques: Microfluidic platforms can be integrated with other analytical tools or techniques, such as mass spectrometry, next-generation sequencing, or imaging modalities, enhancing their capabilities and enabling comprehensive characterization of single cells. Overall, the multifaceted capabilities of microfluidic platforms in single-cell analysis are pivotal in deciphering the complex biological dynamics inherent in individual cells [21]. Their contributions span various domains of research, including fundamental biology, disease mechanisms, drug development, and personalized medicine, offering a deeper understanding of cellular behaviors and functions [22].

3. Conclusion

In conclusion, the integration of nanostructured surfaces within microfluidic systems stands as a transformative approach in the realm of biomolecule manipulation. The synergy between nanotechnology and microfluidics has unveiled a myriad of possibilities, significantly enhancing the efficiency, precision, and control of biomolecules. Nanostructured surfaces play a pivotal role by influencing fluid behavior, promoting selective biomolecular interactions, optimizing mass transport, and offering a platform for multifunctionality. These surfaces offer tailored modifications at the nanoscale, enabling advancements in biomolecular separation, sensing, diagnostics, and drug delivery. The insights garnered from the interplay between nanostructured surfaces and microfluidic transport not only expand our fundamental understanding but also pave the way for innovative technologies poised to revolutionize biomedical research and medical applications. The transformative potential of nanostructured surfaces in augmenting microfluidic transport for efficient biomolecule manipulation holds promise in shaping the future landscape of biotechnology, driving advancements in precision medicine, diagnostics, and therapeutic interventions.

Reference

- [1] C. M. Legner, G. L. Tylka, and S. Pandey, "Robotic agricultural instrument for automated extraction of nematode cysts and eggs from soil to improve integrated pest management," *Scientific Reports*, vol. 11, no. 1, p. 3212, 2021.
- [2] R. Vaidyanathan, S. Dey, L. G. Carrascosa, M. J. Shiddiky, and M. Trau, "Alternating current electrohydrodynamics in microsystems: Pushing biomolecules and cells around on surfaces," *Biomicrofluidics*, vol. 9, no. 6, 2015.
- [3] D. Gao, F. Jin, M. Zhou, and Y. Jiang, "Recent advances in single cell manipulation and biochemical analysis on microfluidics," *Analyst*, vol. 144, no. 3, pp. 766-781, 2019.
- [4] Z. Njus *et al.*, "Flexible and disposable paper-and plastic-based gel micropads for nematode handling, imaging, and chemical testing," *APL bioengineering*, vol. 1, no. 1, 2017.
- [5] K. E. Bates and H. Lu, "Optics-integrated microfluidic platforms for biomolecular analyses," *Biophysical journal*, vol. 110, no. 8, pp. 1684-1697, 2016.

- [6] Y.-C. Li *et al.*, "Manipulation and detection of single nanoparticles and biomolecules by a photonic nanojet," *Light: Science & Applications*, vol. 5, no. 12, pp. e16176-e16176, 2016.
- [7] X. Ding, Z. Njus, T. Kong, W. Su, C.-M. Ho, and S. Pandey, "Effective drug combination for Caenorhabditis elegans nematodes discovered by output-driven feedback system control technique," *Science advances*, vol. 3, no. 10, p. eaao1254, 2017.
- [8] Y. Lai *et al.*, "Recent advances in TiO2-based nanostructured surfaces with controllable wettability and adhesion," *small*, vol. 12, no. 16, pp. 2203-2224, 2016.
- [9] J. T. Luo, N. Geraldi, J. Guan, G. McHale, G. Wells, and Y. Q. Fu, "Slippery liquid-infused porous surfaces and droplet transportation by surface acoustic waves," *Physical Review Applied*, vol. 7, no. 1, p. 014017, 2017.
- [10] U. Kalwa, C. Legner, E. Wlezien, G. Tylka, and S. Pandey, "New methods of removing debris and high-throughput counting of cyst nematode eggs extracted from field soil," *PLoS One*, vol. 14, no. 10, p. e0223386, 2019.
- [11] R. S. Rikken, R. J. Nolte, J. C. Maan, J. C. van Hest, D. A. Wilson, and P. C. Christianen, "Manipulation of micro-and nanostructure motion with magnetic fields," *Soft matter*, vol. 10, no. 9, pp. 1295-1308, 2014.
- [12] J. A. Carr, R. Lycke, A. Parashar, and S. Pandey, "Unidirectional, electrotactic-response valve for Caenorhabditis elegans in microfluidic devices," *Applied Physics Letters*, vol. 98, no. 14, 2011.
- [13] C.-W. Lee and F.-G. Tseng, "Surface enhanced Raman scattering (SERS) based biomicrofluidics systems for trace protein analysis," *Biomicrofluidics*, vol. 12, no. 1, 2018.
- [14] S. O. Kelley, C. A. Mirkin, D. R. Walt, R. F. Ismagilov, M. Toner, and E. H. Sargent, "Advancing the speed, sensitivity and accuracy of biomolecular detection using multi-length-scale engineering," *Nature nanotechnology*, vol. 9, no. 12, pp. 969-980, 2014.
- [15] T. Kong, N. Backes, U. Kalwa, C. Legner, G. J. Phillips, and S. Pandey, "Adhesive tape microfluidics with an autofocusing module that incorporates CRISPR interference: applications to long-term bacterial antibiotic studies," *ACS sensors*, vol. 4, no. 10, pp. 2638-2645, 2019.
- [16] L. Li, C. Wang, Y. Nie, B. Yao, and H. Hu, "Nanofabrication enabled lab-on-a-chip technology for the manipulation and detection of bacteria," *TrAC Trends in Analytical Chemistry*, vol. 127, p. 115905, 2020.
- [17] J. Chen *et al.*, "Optothermophoretic flipping method for biomolecule interaction enhancement," *Biosensors and Bioelectronics*, vol. 204, p. 114084, 2022.
- [18] A. Q. Beeman, Z. L. Njus, S. Pandey, and G. L. Tylka, "The effects of ILeVO and VOTiVO on root penetration and behavior of the soybean cyst nematode, Heterodera glycines," *Plant disease*, vol. 103, no. 3, pp. 392-397, 2019.
- [19] S. Bai, X. Ren, K. Obata, Y. Ito, and K. Sugioka, "Label-free trace detection of bio-molecules by liquid-interface assisted surface-enhanced Raman scattering using a microfluidic chip," *Opto-Electronic Advances*, vol. 5, no. 10, pp. 210121-1-210121-10, 2022.
- [20] J. P. Jensen, U. Kalwa, S. Pandey, and G. L. Tylka, "Avicta and Clariva affect the biology of the soybean cyst nematode, Heterodera glycines," *Plant disease*, vol. 102, no. 12, pp. 2480-2486, 2018
- [21] Y. Ren, Q. Chen, M. He, X. Zhang, H. Qi, and Y. Yan, "Plasmonic optical tweezers for particle manipulation: principles, methods, and applications," *ACS nano*, vol. 15, no. 4, pp. 6105-6128, 2021.
- [22] A. Parashar and S. Pandey, "Plant-in-chip: Microfluidic system for studying root growth and pathogenic interactions in Arabidopsis," *Applied physics letters*, vol. 98, no. 26, 2011.