

From: JPGT - Editorial Office <em@editorialmanager.com>

To: Yong-Jin Yoon <yongjiiny@kaist.ac.kr>

Sent: 2025-06-25T18:49:31+09:00

Subject: Major Revisions requested JPGT-D-25-00212

Dear Dr. Yoon,

We have received the reports from our advisors on your manuscript, 'Acoustofluidics Lab on a chip system for size-based nanoparticle separation', which you submitted to International Journal of Precision Engineering and Manufacturing-Green Technology.

Based on the advice received, I have decided that your manuscript could be reconsidered for publication should you be prepared to incorporate major revisions. When preparing your revised manuscript, you are asked to carefully consider the reviewer comments which can be found below, and submit a list of responses to the comments. You are kindly requested to also check the website for possible reviewer attachment(s).

In order to submit your revised manuscript, please access the following web site:

Your username is: yongjiiny

If you forgot your password, you can click the 'Send Login Details' link on the EM Login page at <https://www.editorialmanager.com/jpgt/>.

Please note: When uploading your revised manuscript files, please make sure only to submit your editable source files (i.e. Word, Tex). PDF is not allowed at this stage.

We look forward to receiving your revised manuscript before 23 Jul 2025.

With kind regards,

Suk Won Cha

Editor in Chief

International Journal of Precision Engineering and Manufacturing-Green Technology

COMMENTS FOR THE AUTHOR:

Reviewer #1: 1. Authors should be revise Abstract. Authors should supplement the novelty and the objective of the paper in the Abstract.

2. It is necessary to enhance the resolution of all figures. In addition, the font size in the figures should also be increased to improve understanding of readers.

3. In the content and figure caption, Figure should be change to Fig..

4. Figure captions should be thoroughly revised to conform to the format of IJPEM-GT. Could you revise the figure captions by referring to those in previously published papers in IJPEM-GT?

Reviewer #2: The authors presents a well-designed acoustofluidic lab-on-a-chip system that effectively addresses key challenges in size-based nanoparticle separation for point-of-care applications. The integration of ultrasonic agitation (28-40 kHz) with dead-end membrane filtration is a compelling

innovation, demonstrating significant improvements in separation efficiency and recovery rates. The authors convincingly show that ultrasound prevents cake-layer formation and reverses fouling, achieving a 70% recovery rate for 60 nm Au nanoparticles—a substantial improvement over non-ultrasonic methods. The fabrication approach using commercially available track-etched membranes and straightforward PDMS prototyping enhances practicality and accessibility. Experimental validation through UV-Vis spectroscopy, DLS, and fluorescence imaging is thorough, with particularly valuable insights into the critical role of membrane wetness and ultrasonic transducer orientation (feed-side irradiation proving superior).

However, the manuscript would benefit from clarifying the scalability of recovery rates beyond the 60 nm Au NP model, especially for biological targets like monosomes. While the 70% recovery is impressive, sample loss remains notable, warranting further optimization. Additionally, comparative data with existing separation techniques would strengthen the case for this platform's superiority. The conclusions about POC suitability feel slightly premature without validation in complex biological matrices. Overall, this work makes a valuable contribution to microfluidic separation technology with strong experimental foundations, though translational readiness requires further biological validation and loss reduction strategies.

Editor's note: IJPEM-GT encourages the authors to refer IJPEM and IJPEM-GT articles. Please consider referring recent IJPEM and IJPEM-GT articles in the revised manuscript.

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To Dr. Suk Won Cha, the Editor in Chief

We thank the Editor and the other reviewer for putting their efforts. Based on their comments, we have made significant changes to our original submission. The attached transmittal letter (**Rebuttal_major.pdf**) contains the reviewers' and editor's comments, followed by the authors' response in blue. We look forward to hearing from you soon.

Sincerely,

Yong-Jin Yoon, Ph.D.

Professor / KAIST ME

Visiting Professor / NTU MAE

Chairman/ University Industrial Technology Force (UNITEF.org)

Director / Center for Drone Defense Industry

Editor's note

IJPEM-GT encourages the authors to refer IJPEM and IJPEM-GT articles. Please consider referring recent IJPEM and IJPEM-GT articles in the revised manuscript.

Thank you so much for the constructive comments to align our manuscript more suitable for prestigious IJPEM and IJPEM-GT journals. We tried to add more articles and added four more references to broadly include the relevant Lab-on-Chip approach in the fields of MEMS. It seems there are no previous efforts about nanoparticle separations or acoustofluidics in IJPEM and IJPEM-GT. We are confident that our manuscript will add additional spectrum to these journals to add more impact to Lab-on-Chips aims, specifically "4 Materials for Green Manufacturing - Micro-/Nano-materials for Green Applications"

The newly added references are listed here and also highlighted in our resubmission.

- Xu, J., Hong, H., Wang, Z., Sun, X., Wei, Y., & Liu, Y.: Multiscale Prototyping Approach via In-situ Switching Electrohydrodynamics for Flexible Microfluidic Design. *International Journal of Precision Engineering and Manufacturing-Green Technology*, 11(2), 353-364 (2024). <https://doi.org/10.1007/s40684-023-00543-2>
- Kim, S., Kim, D. H., Kim, W., Cho, Y. T., & Fang, N. X.: Additive manufacturing of functional microarchitected reactors for energy, environmental, and biological applications. *International Journal of Precision Engineering and Manufacturing-Green Technology*, 8(1), 303-326 (2021). <https://doi.org/10.1007/s40684-020-00277-5>
- Roos, M. M., Winkler, A., Nilsen, M., Menzel, S. B., & Strehle, S.: Towards green 3D-microfabrication of Bio-MEMS devices using ADEX dry film photoresists. *International Journal of Precision Engineering and Manufacturing-Green Technology*, 9(1), 43-57 (2022). <https://doi.org/10.1007/s40684-021-00367-y>
- Sharma, A., Mondal, S., Mondal, A. K., Baksi, S., Patel, R. K., Chu, W. S., & Pandey, J. K.: 3D printing: It's microfluidic functions and environmental impacts. *International Journal of Precision Engineering and Manufacturing-Green Technology*, 4, 323-334 (2017). <https://doi.org/10.1007/s40684-017-0038-6>

Also refer to our manuscript pages 4 and 5 for relevant updates:

"Furthermore, most passive separation techniques necessitate expensive microfabrication. For point-of-care applications, a lab-on-chip system is required that can be realized through a simple fabrication process, offers a user-friendly interface for easy sample handling, and yet achieves high resolution with minimal sample loss [33-35]. "

"When acoustic waves are employed to manipulate fluids or particles at the micro- and nanoscale, the field is known as acoustofluidics. Its applications are vast, spanning from fundamental physics to advanced engineering."

These changes are highlighted in our resubmission in red.

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Thank you so much for this information. All authors understand the points addressed above and will comply the terms and conditions of journal regarding the funder and institutional open access mandates. We checked the website and found the following information.

If you're affiliated with the Korea Advanced Institute of Science and Technology (KAIST), you can publish your article open access with fees covered in journals across the Springer Nature portfolio. Starting 01 January 2024, if you're a corresponding author affiliated with KAIST, you can publish

open access (OA) with fees covered in Springer Nature's portfolio of hybrid journals. As part of the agreement, you will be able to read, use and reuse research published in over 2,000 Springer Nature journals across the Springer, Palgrave Macmillan, Adis and in the Academic Journals on nature.com. <https://www.springernature.com/gp/open-science/oa-agreements/south-korea/korea-advanced-institute-of-science-and-technology>

As Prof. Yoon is from KAIST, we can confirm that we can publish our manuscript as OA with coverage. Thank you again for this information.

Reviewer 1

1. Authors should be revise Abstract. Authors should supplement the novelty and the objective of the paper in the Abstract.

Thank you for taking the time to review our manuscript. We agree that we missed highlighting the novelty and objective of the paper in the abstract. Based on your constructive comments, we've carefully revised our abstract, and the changes are highlighted in red below (also available in the resubmission package). Additionally, we've refined the entire text for improved flow, conciseness, and impact, ensuring every sentence contributes clearly to the overall message without repetition.

"Despite the growing demand for nanoscale biomolecule analysis in point-of-care (POC) applications, nanoparticle separation remains a significant challenge. This is due to issues like high sample loss, low throughput, large-scale material requirements, and the complexity of current technologies. Given that separation efficiency directly impacts subsequent sample processing and analysis, there is a clear need for a robust and reliable size-based separation technique. This study introduces a novel acoustofluidics lab-on-a-chip system designed to overcome current separation barriers. It combines simple polymer prototyping with integrated ultrasonic agitation. The system features two key components: (1) a microfluidic network embedded with membrane filters of varying pore-size cut-offs, and (2) an ultrasonic transmitter that induces acoustic agitation. Using this novel system, we successfully demonstrate the fractionation of 60 nm Au nanoparticles from a polydisperse solution under ultrasonic waves (28-40 kHz) generated by the transducer integrated into the microfluidic platform. Ultrasonic irradiation not only prevents cake formation but also reverses the fouling process through acoustic agitation. This significantly increases the flow rate during separation and improves the recovery of target-size nanoparticles. This microfluidic platform holds great potential as a powerful tool for sample preparation and analytical methodologies in POC applications. "

2. It is necessary to enhance the resolution of all figures. In addition, the font size in the figures should also be increased to improve understanding of readers.
[Check our answers combined below after your comment 4.](#)
3. In the content and figure caption, Figure should be change to Fig..
[Check our answers combined below after your comment 4.](#)
4. Figure captions should be thoroughly revised to conform to the format of IJPEM-GT. Could you revise the figure captions by referring to those in previously published papers in IJPEM-GT?

Our answers for the reviewer's comments 2-4 on the figures are combined here: We greatly appreciate your feedback regarding the figures. In response, we have revisited all nine figures in our manuscript, significantly enhancing their resolution and optimizing font sizes for improved readability and precision. To fully comply with IJPEM-GT's figure practices, we've also ensured that all figures are consistently cited as "Fig." throughout the text and have meticulously reworked every figure caption and relevant languages to align with the journal's specific style guidelines. Please do not hesitate to inform us if you have any additional concerns about the figures.

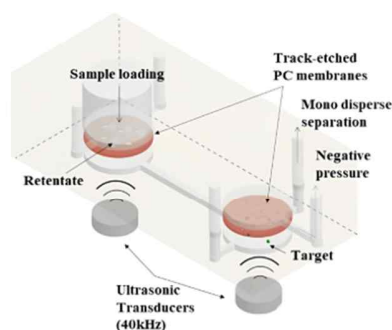


Fig.1 Schematic of a microfluidic platform for nanoparticle separation.

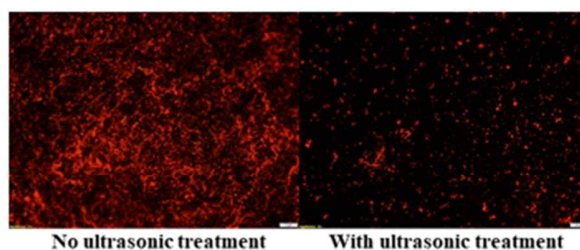


Fig. 2 Effect of ultrasonic treatment during NP separation

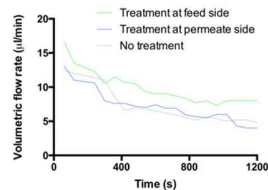
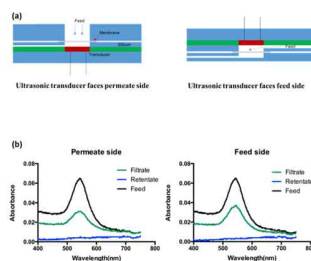
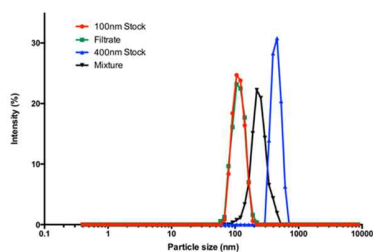
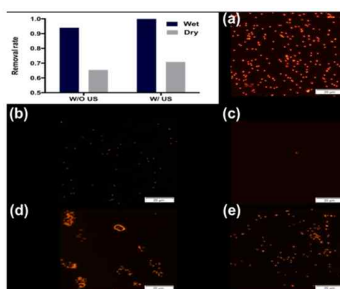
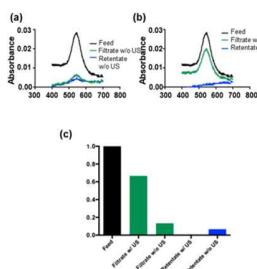
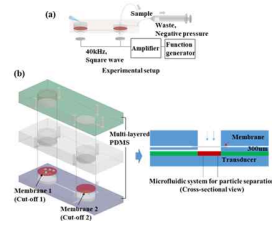
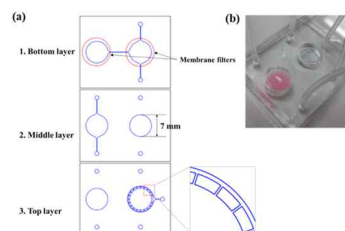


Fig. 9 Volumetric flow rate of sample filtered using microfluidic particle separation system as a function of filtration time

Thank you very much for your consideration. As stated above, we put our best effort into improving our manuscript, especially in terms of abstraction, writing quality, and substantiation of our results. Kindly let us know if you have further comments on our revision.

Reviewer 2

The authors presents a well-designed acoustofluidic lab-on-a-chip system that effectively addresses key challenges in size-based nanoparticle separation for point-of-care applications. The integration of ultrasonic agitation (28-40 kHz) with dead-end membrane filtration is a compelling innovation, demonstrating significant improvements in separation efficiency and recovery rates. The authors convincingly show that ultrasound prevents cake-layer formation and reverses fouling, achieving a 70% recovery rate for 60 nm Au nanoparticles—a substantial improvement over non-ultrasonic methods. The fabrication approach using commercially available track-etched membranes and straightforward PDMS prototyping enhances practicality and accessibility. Experimental validation through UV-Vis spectroscopy, DLS, and fluorescence imaging is thorough, with particularly valuable insights into the critical role of membrane wetness and ultrasonic transducer orientation (feed-side irradiation proving superior).

Your summary captures the essence of our work. Thank you so much for recognizing our achievement.

However, the manuscript would benefit from clarifying the scalability of recovery rates beyond the 60 nm Au NP model, especially for biological targets like monosomes. While the 70% recovery is impressive, sample loss remains notable, warranting further optimization. Additionally, comparative data with existing separation techniques would strengthen the case for this platform's superiority. The conclusions about POC suitability feel slightly premature without validation in complex biological matrices.

Thank you for your insightful comments regarding the scalability, recovery rates, comparative data, and point-of-care suitability of our platform. We completely agree that these are crucial aspects to address for the full realization of our technology's potential.

In response, we have incorporated a dedicated section within our Conclusion as "Limitations and Future Work" of our current work that directly addresses these points. We explicitly state that future work will focus on:

"While this study successfully demonstrates the promise of our acoustofluidics platform for nanoparticle separation, we acknowledge certain limitations and identify clear avenues for future work. Our current findings, particularly the 70% recovery rate, are primarily based on 60 nm Au nanoparticles. Future research will focus on clarifying the scalability of these recovery rates to a broader range of biological targets, such as monosomes, and further optimizing the system to minimize sample loss. Additionally, to solidify the platform's advantages for point-of-care (POC) applications, future efforts will include rigorous comparative studies with existing separation techniques and validation experiments within complex biological matrices. These advancements will be crucial for fully realizing its potential in real-world POC settings."

We believe this addition provides a balanced perspective on the current work while outlining a clear roadmap for future research, directly acknowledging the valuable concerns you raised.

Overall, this work makes a valuable contribution to microfluidic separation technology with strong experimental foundations, though translational readiness requires further biological validation and loss reduction strategies.

We deeply appreciate your inputs. Do not hesitate to let us know if you have further suggestions regarding to our resubmitted manuscript. Thank you for your time and consideration. We look forward to hearing from you soon.