Directed Assembly of Microscale Particles by Acoustic Waves for Biomedical Applications

Feng Xu [a], Umut A. Gurkan [a], Thomas D. Finley [a], Müge Türkaydın [a], Ahmet S. Yavuz [a], Onur Hasan, Utkan Demirci [a,b#]
[a] Bio-Acoustic-MEMS in Medicine (BAMM) Laboratory, Center for Biomedical Engineering, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[b] Harvard-MIT Health Sciences and Technology, Cambridge, MA, USA.
[#] Corresponding author: udemirci@rics.bwh.harvard.edu

Statement of Purpose: Directed assembly of microgels holds great potential for applications in tissue engineering and regenerative medicine. Large gel patterns have been achieved with controlled features (*e.g.*, shape, size, spatial resolution). However, there are several limitations associated with the existing techniques (hydrophilic-hydrophobic interactions [1, 2], surface template [3, 4]) such as complexity of assembly process, involvement of organic solvents. There is still an unmet need for straightforward assembly methods.

Acoustic techniques, *e.g.*, ultrasonic standing waves and acoustic droplet based bioprinting are emerging technologies, especially when integrated with microfluidics [5, 6]. The acoustic technology offers several advantages such as decreased instrumentation complexity and gentler handling of pressure and heat sensitive biological moieties such as cells [7, 8]. However, acoustics have not been used for microgel assembly.

Methods: In this study we have developed a novel acoustic assembler to assemble microscale hydrogels, **Figure 1a**. Microgels (PEG, MW 1000) of different shapes were fabricated using photolithography. The microgels were subjected to plasma treatment to give the surfaces hydrophilic properties that allow enhanced mobility before acoustic assembly. The treated microgels were deposited onto the hydrophobic surface of a petri dish where 40µL of deionized water was added to the group of microgels. The petri dish was placed above a piezo buzzer (Digi-Key, CPE-827) and exposed to acoustic vibrations produced by a pulse/function generator.

Results: To evaluate particle manipulation with our acoustic assembler, we assembled glass microbeads (**Figure 1b-c**) and microgels with different shapes (**Figure 1d-e)**. After applying acoustic excitation, the microbeads came together at the center of the droplet within 30 sec, **Figure 1b**. We observed that the microbeads assembly time was dependent on excitation frequency, **Figure 1c**. During acoustic excitation, we observed that some microgels were immobile due to settling on their untreated surface. It was determined that a frequency sweep provoked mobility in the microgels more so than using a constant frequency, leading to the assembly of orientation specific microgels, **Figure 1d-e**.

Conclusions: In this study we report an acoustic assembler that utilizes microscale hydrogels as building blocks to create larger constructs via external acoustic fields. This approach has potential to impact multiple fields including tissue engineering, regenerative medicine, and pharmacology.

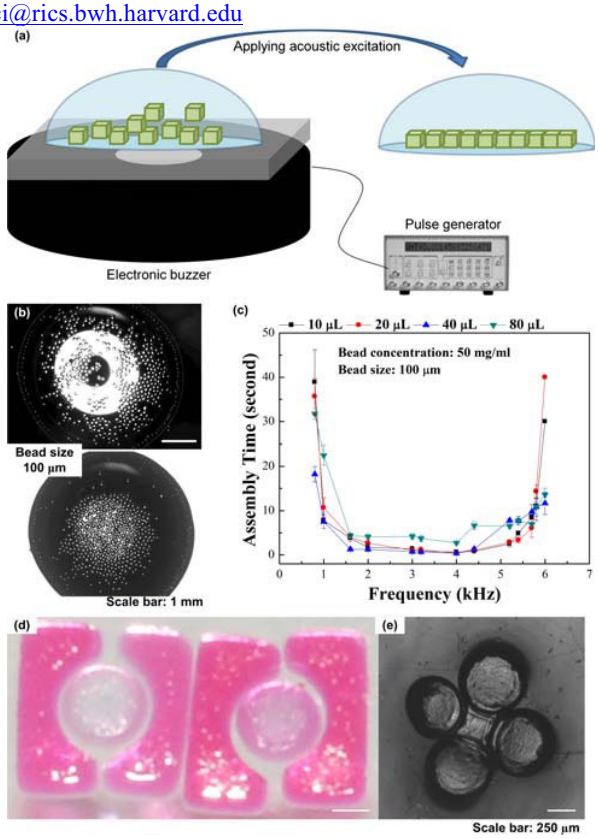

Figure 1. Acoustic directed assembly of microbeads and microgels. (a) Schematic of the developed acoustic assembler; **(b)** Images of microbeads in a droplet before and after acoustic excitation; **(c)** Effect of acoustic generation frequency and droplet size on bead assembly time; **(d)-(e)** Assembled microgels.

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