Microfluidic Acoustic Methods

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BACKGROUND

The use of standing surface acoustic waves (SSAWs) in microfluidic channels gained significant momentum when researchers demonstrated size-based cell separation (acoustophoresis) using lateral acoustic forces. Using interdigitated transducers (IDTs) positioned on piezoelectric substrates, SSAWs were found to create pressure nodes along the channel width, allowing larger particles to experience greater acoustic radiation forces and migrate toward these nodes faster than smaller particles. Acoustic-based microfluidic devices were successfully applied to circulating tumor cell (CTC) isolation from clinical blood samples in ~2015, demonstrating recovery rates >80% using tilted-angle standing surface acoustic waves, though these systems relied primarily on size-based separation principles. The integration of acoustic methods with microfluidics offered key advantages including label-free operation, biocompatibility, non-contact manipulation, and preservation of cell viability, addressing limitations of earlier methods like centrifugation, FACS, and magnetic separation that could damage cells or require labeling. Despite these advances in acoustic microfluidics, significant challenges persist in affinity-based rare cell isolation, particularly mass transport limitations in microfluidic channels operating at high Peclet numbers ($Pe>10^6$) where convective flow dominates over diffusion. In traditional microfluidic affinity capture systems, cells flow predominantly in the center of laminar flow channels where fluid velocity is highest, resulting in minimal interaction with capture agents immobilized on channel walls and requiring extremely long channels or impractically slow flow rates to achieve adequate capture efficiency. The extremely low concentration of CTCs , combined with their phenotypic heterogeneity and the low diffusion coefficients of cells creates a "needle in a haystack" challenge that existing acoustic separation methods based solely on size discrimination cannot adequately address.

TECHNOLOGY DESCRIPTION

To help address these challenges with SSAW microfluidics "needle in a haystack" (e.g., approximately 1 cell per billion blood cells, or fewer than 1 CTC per 10 mL in early-stage cancer), researchers at UC Santa Cruz (UCSC) have developed approach based on the Acoustic Drifting Effect (ADE). This technology based on ADE differs from conventional surface acoustic wave (SAW) acoustophoresis by generating a vertical acoustic radiation force perpendicular to the flow direction rather than lateral forces along the channel width. By engineering an acoustic cavity formed between a piezoelectric substrate and an elastic polydimethylsiloxane (PDMS) channel ceiling, the SAWs generate compressional bulk acoustic waves (BAWs) that undergo multiple reflections, creating a quasi-standing wave in the vertical direction composed of both gradient and scattering acoustic radiation force components. The vertical force field drives particles downward toward the piezoelectric substrate surface where capture agents are immobilized, decoupling mass transport from microfluidic flow and enabling high-efficiency affinity capture (approaching 90% capture efficiency) and at high flow rates (up to 4.8 mL/hr) and challenging conditions ($Pe>10^6$, Re~0.18-0.54) without disrupting laminar flow profiles. This represents an order of magnitude improvement in mixing distance and two orders of magnitude improvement in handling particles with smaller diffusion coefficients compared to previous milestone work. The lab device research resulted in successful capture of biotin-functionalized particles on avidin-coated surfaces with minimal non-specific binding, and completed the capture process within channel regions shorter than 2mm, while also enabling acoustic release of captured cells through heat-mediated bond neutralization and acoustic pressure application.

APPLICATIONS

- liquid biopsy diagnostics, e.g., isolation of rare CTCs
- stem cell research and therapy, e.g., high-purity isolation of stem cells, endothelial progenitor cells
- immunotherapy, e.g., enrichment of specific T-cell populations
- prenatal diagnostics, e.g., isolation of fetal cells

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OTHER INFORMATION

KEYWORDS

acoustic drifting effect, standing surface acoustic wave, microfluidic, microfluidics, surface acoustic wave, microfluidic acoustic device, liquid biopsy, acoustophoresis, acoustic-based microfluidic device, acoustic microfluidics, circulating tumor cell

CATEGORIZED AS

- Biotechnology
  - Other
- Medical
  - Other
- Research Tools
  - Other
- Sensors & Instrumentation
  - Other
  - Scientific/Research
- Engineering
  - Other

RELATED CASES

2017-681-0

FEATURES/BENEFITS

- Addresses gaps in existing acoustic separation methods based solely on size discrimination; achieves separation for CTCs with sizes similar to white blood cells.
- Decouples mass transport from fluid flow, enabling high-throughput (up to 4.8 mL/hr) and high capture efficiency (~90%).
- Provides two-stage enrichment combining size-based separation (removing RBCs and platelets) with high-specificity affinity capture.
- Optimizes particle movement toward capture surface while maintaining laminar flow and minimizing shear stress damage to cells.

INTELLECTUAL PROPERTY INFORMATION

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,668,676	06/06/2023	2017-681

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Neuro-Swarm3: System-On-A-Nanoparticle For Wireless Recording Of Brain Activity
- Plasmofluidic Microlenses for Label-Free Optical Sorting of Bioparticles

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