Miniature Flow Cytometer for Medical Diagnostics and Pathogen Detection

LABORATORY DIRECTED RESEARCH & DEVELOPMENT

Sandia National Laboratories

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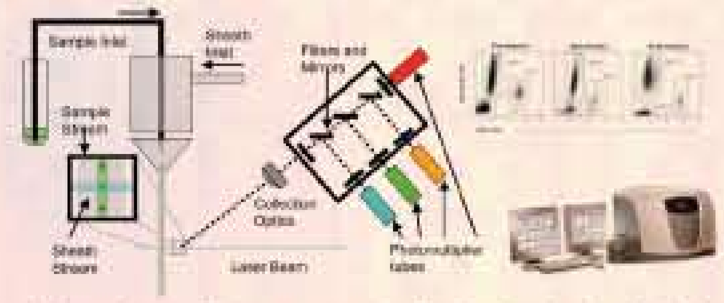
Introduction to Flow Cytometry



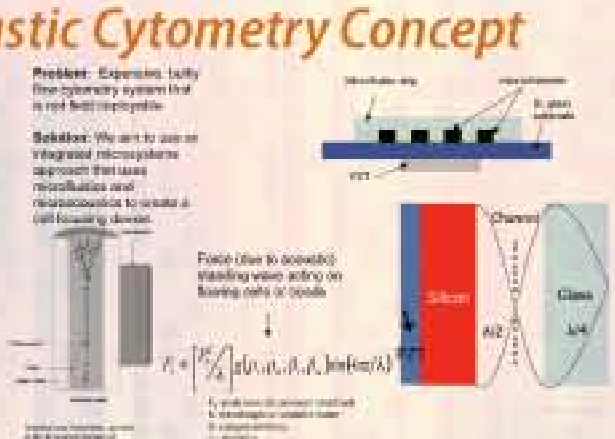
- An analysis tool for understanding & measuring biochemical and physical properties of cells, i.e., protein levels.
- Specific receptors or proteins are fluorescently labeled.
- Separate sheath flow focuses cells into a single-file line.
- Single or multiple laser beams excite fluorescence and/or scattering. Fluorescent intensity is then correlated with receptor levels or protein expression.

Why Miniature Cytometry at Sandia?

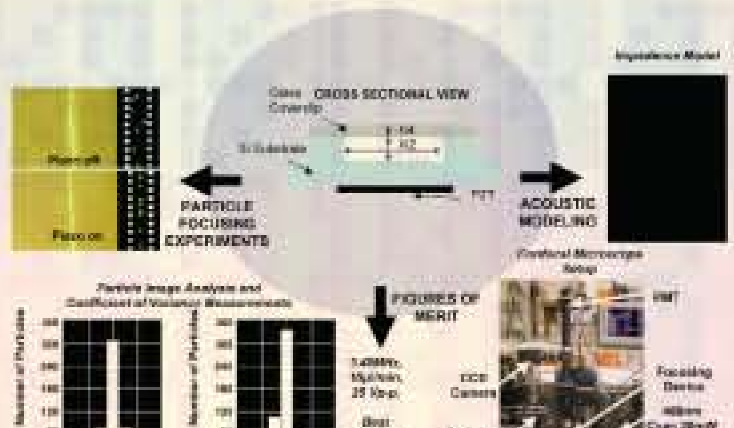
- National Security
  - It is the gold standard for microsphere-based assays.
  - Has been used for biothreat I.D. as the back-end detector in PCR-based devices.
- Clinical diagnostics in civilian and military clinics
  - It is the gold standard for infectious disease diagnostics.
  - Bio-attacks, AIDS, anemia, cancer, and many infectious diseases.
  - Assays can be multiplexed, saving time and sample size.
  - Credible replacement for ELISA.

Autonomous Pathogen Detection System (APDS), LLNL

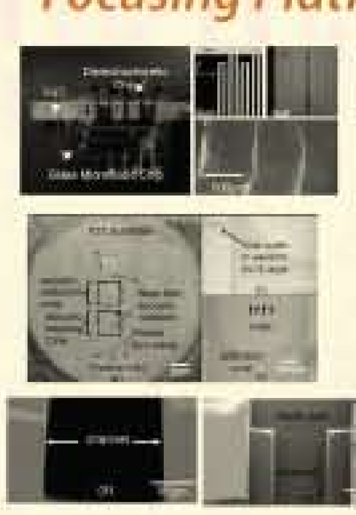
Microacoustic Cytometry Concept



Overview of Approach and Results



Fabrication Paradigms for Microacoustic Focusing Platforms



Key Features

- Integration of acoustics with dielectrophoresis to achieve highly focused streams
- Use of glass-glass thermal bonding for optical access to channels

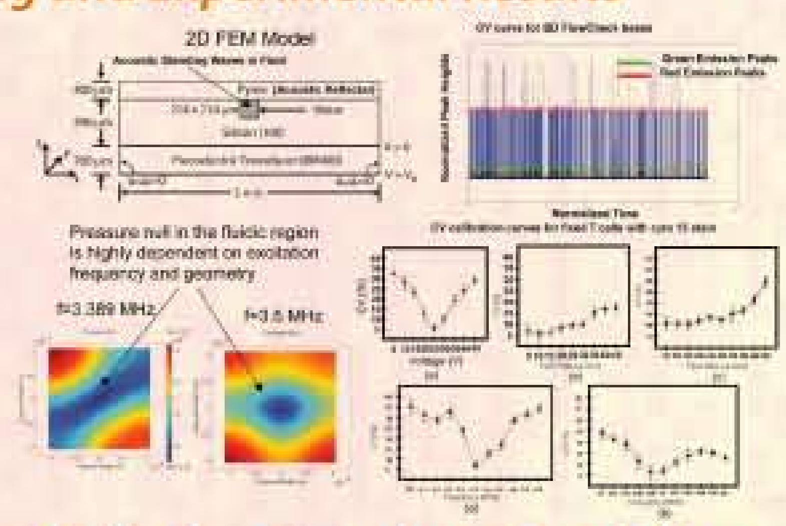
Key Features

- Particles focused hydrodynamically along the width and acoustically along the height of the microchannels
- Integration of an acoustic sorter along with the focusing
- Fabricated on a bulk piezo substrate and channels created out of a multilayer SU 8 photoresist process

Key Features

- Ease of fabrication
- 2-step Bosch etch process
- Anodic Bonding of glass reflector
- 2-D Focusing with a single PZT transducer

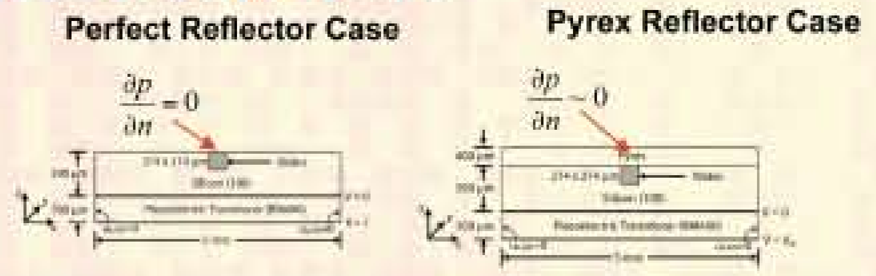
Modeling and Experimental Results



Impact of Reflector Boundary Conditions: Force on Microparticles

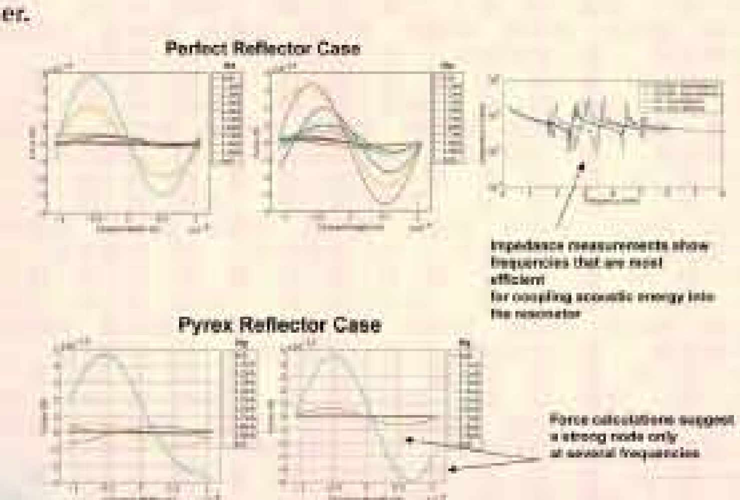
Perfect Reflector Case $\frac{\partial p}{\partial n} = 0$

Pyrex Reflector Case $\frac{\partial p}{\partial n} \sim 0$

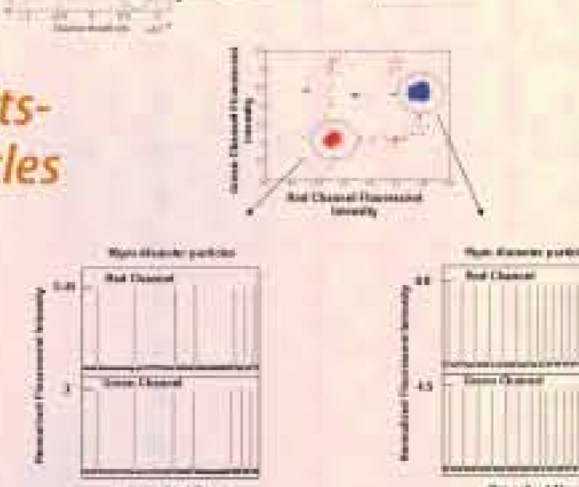


Perfect Reflector: To achieve the best possible acoustic reflection, this boundary condition requires that the normal derivative of the pressure is zero.

Pyrex Reflector: Conventional λ/4 reflectors may cause the normal derivative of the pressure to be non-zero. This causes a reduction in the acoustic reflection and hence standing wave field is weaker.



Experimental Results-Separationof Particles by Size



Summary and Conclusions

- Designed, fabricated, and characterized a microfluidic-acoustic focusing module for flow cytometry.
- Obtained good flow-focusing with microbeads and cells.
- Developed a detailed FEM modeling strategy to serve as a design and analysis tool
- Needs further optoelectronic integration for a complete cytometer-on-a-chip.

Partial List of References

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