# LOCALIZED CELL LYSIS BY SELF FOCUSED ACOUSTIC TRANSDUCERS

Ref[1] : Transducer 2009

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# Outline

- Introduction and paper review
  - + Acoustic underwater thruster (*Ref: MEMS 2004*)
  - + Directional droplet ejection by nozzleless acoustic ejectors built on ZnO and PZT (*Ref: JMM 2006*)
  - + ACOUSTIC EJECTOR WITH NOVEL LENS EMPLOYING AIR-REFLECTORS (*Ref: MEMS 2006*)
- Design and concept
- Fabrication and measurement
- Summary

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# Introduction

- High intensity acoustic wave has long been explored in biomedical engineering for cell lysis and tumor treatment.
- Applications for single cell analysis and tumor treatment require the target cells to be damaged accurately without harming others.
- Conventional acoustic devices are working on a large area with low acoustic frequency, which would affect other cells inevitably
- Localized cell lysis by using Self Focused Acoustic Transducers (SFAT) with a Fresnel lens.

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- Design and concept
  - Self-Focusing Acoustic Transducer (SFAT)
  - Acoustic lens
- Fabrication and measurement
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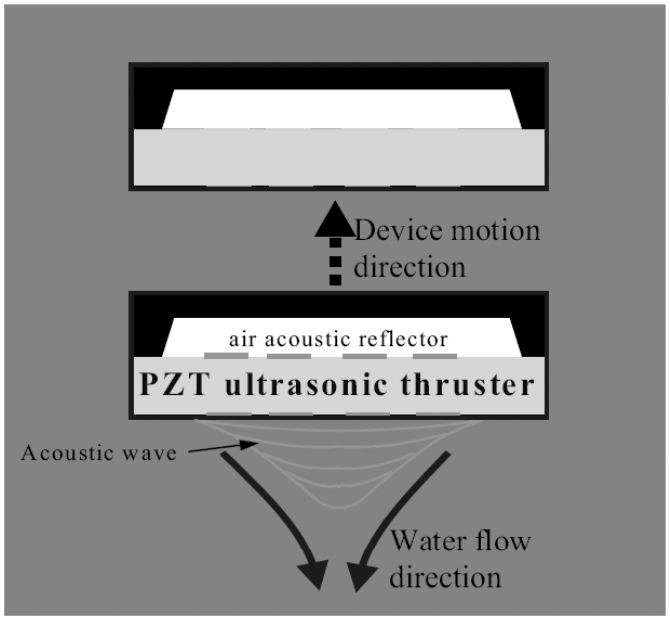
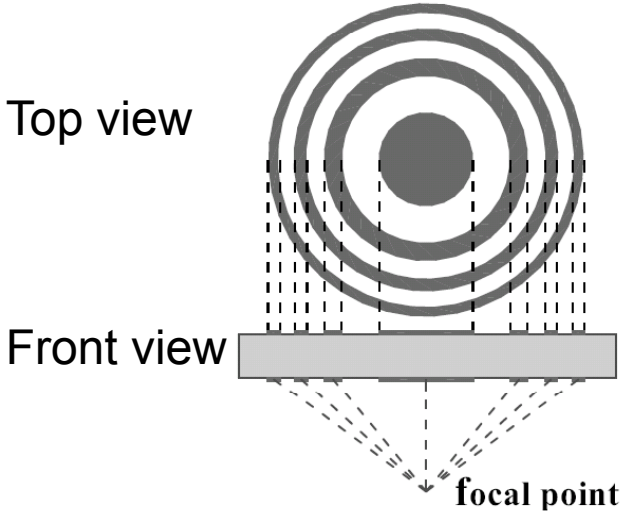
# Acoustic underwater thruster

Ref: MEMS 2004




- An novel ultrasonic underwater thruster without any moving part
- Moves forward by shooting out water jet stream backward through an acoustic streaming effect.
- To enhance the acoustic streaming effect, SFAT is used.

+ thrust ratio of 19:1, (5.6mN:0.3mN)

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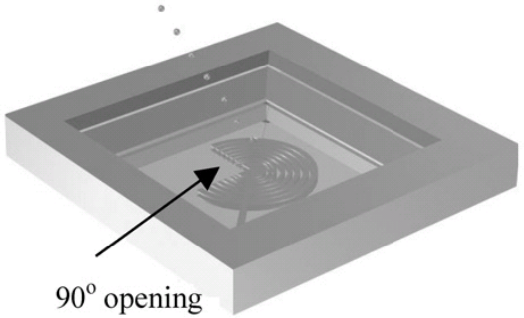
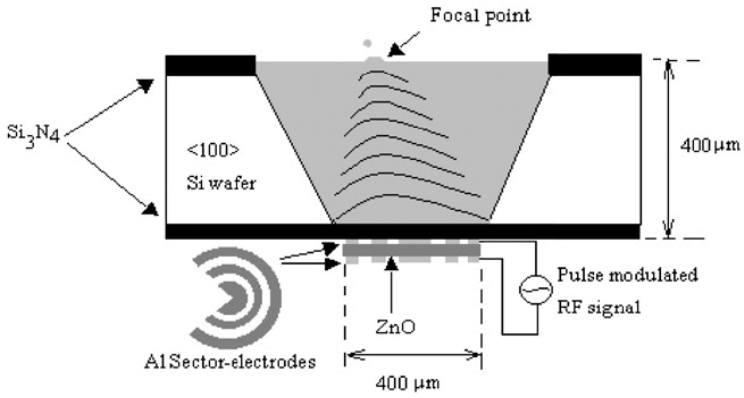
# Directional droplet ejection by nozzleless acoustic ejectors built on ZnO and PZT

Ref: JMM 2006

- Eject liquid droplets in almost any direction with a nozzleless SFAT.

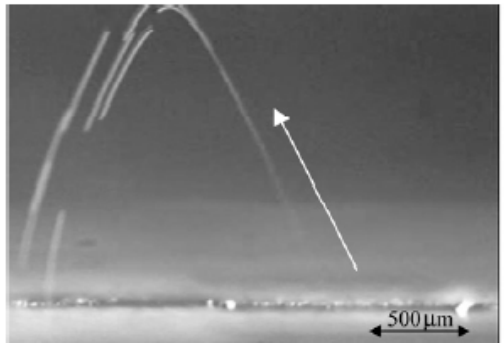



(a)

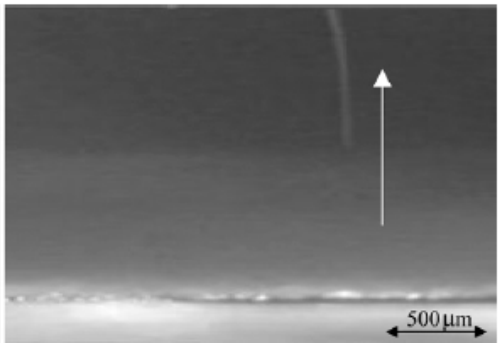



(b)

- Obliquely inclined directional ejection of liquid droplets by a sector SFAT.




+ 270 sector SFAT




+ complete ring SFAT

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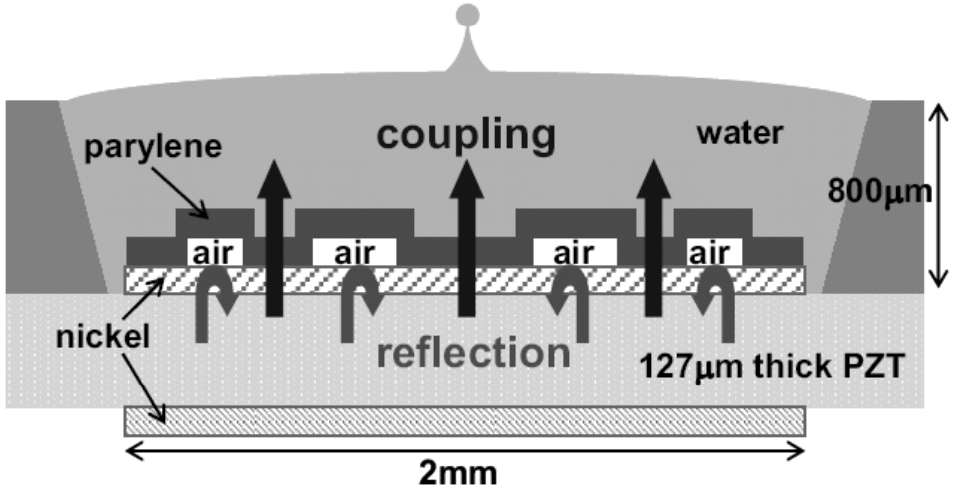
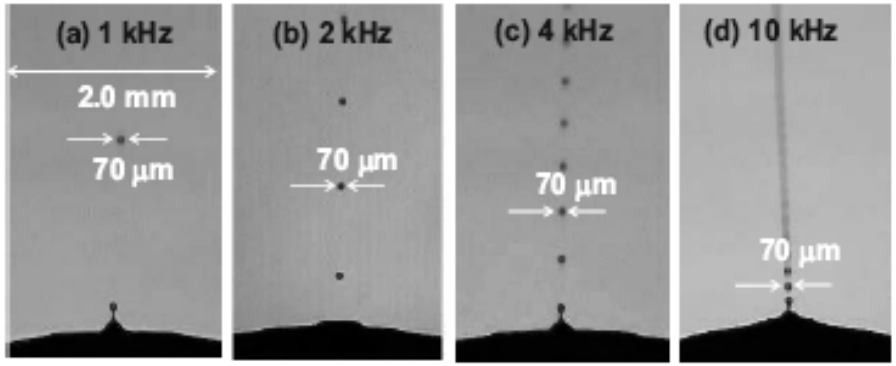
# ACOUSTIC EJECTOR WITH NOVEL LENS EMPLOYING AIR-REFLECTORS

Ref: MEMS 2006

- A novel droplet ejector with an acoustic lens employing air-reflectors.
- Acoustic impedance of air is comparatively infinitesimal
- ejects uniform droplets at a rate up to 10 kHz.



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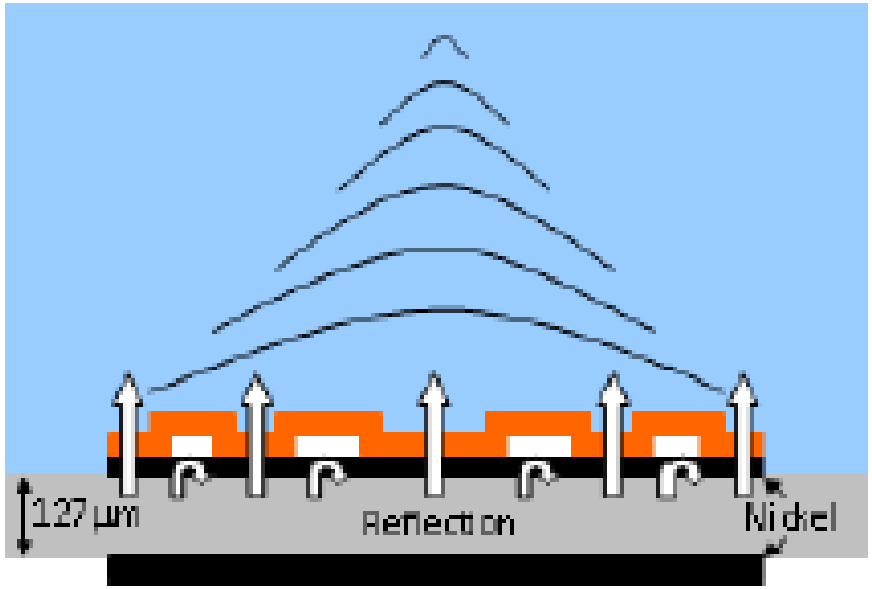
# Self-Focusing Acoustic Transducer (SFAT)

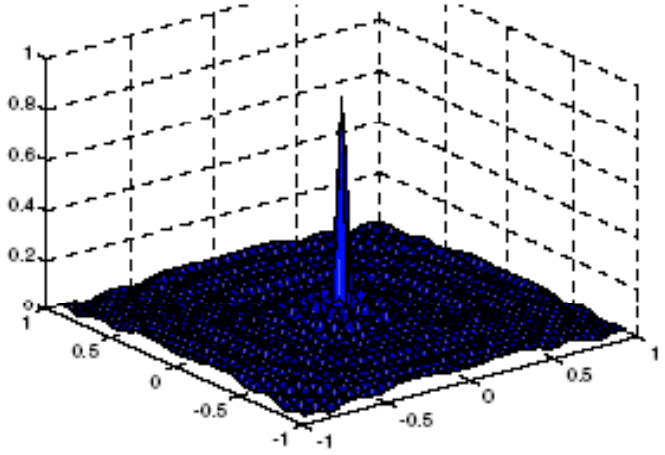
- The transducer consists of a PZT layer (127 m ) and a Fresnel lens.
- The acoustic waves are produced only from electrode-covered areas and propagate into water.




+ PZT sheet working at the thickness mode
+ Fresnel lens are fabricated by
  - (1) patterning Nickel electrodes.
  - (2) using Parylene with air reflectors.

# Self-Focusing Acoustic Transducer (SFAT)

- Acoustic waves transmit through Fresnel lens and arrive at the focal point in phase, constructively interfering with each other,
- Focusing on a small spot with a diameter of around 100 μm, and resulting a very high acoustic intensity.
- The focal distance can be set from 500 μm to 1500 μm depending on lens design.




+To simulate the focal effect of the transducers indicate perfect focusing.

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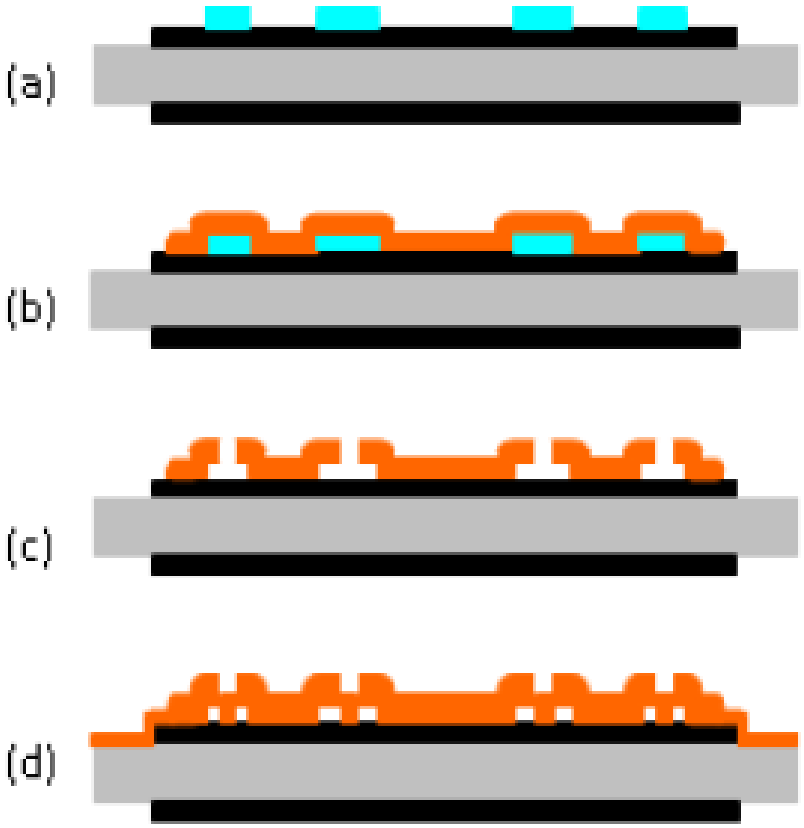
# Fabrication process of air-reflector type of SFAT




+ (a) pattern nickel electrodes on top and bottom of the PZT sheet, followed by coating and patterning of photoresist layer (3 μm) for the sacrificial layer,

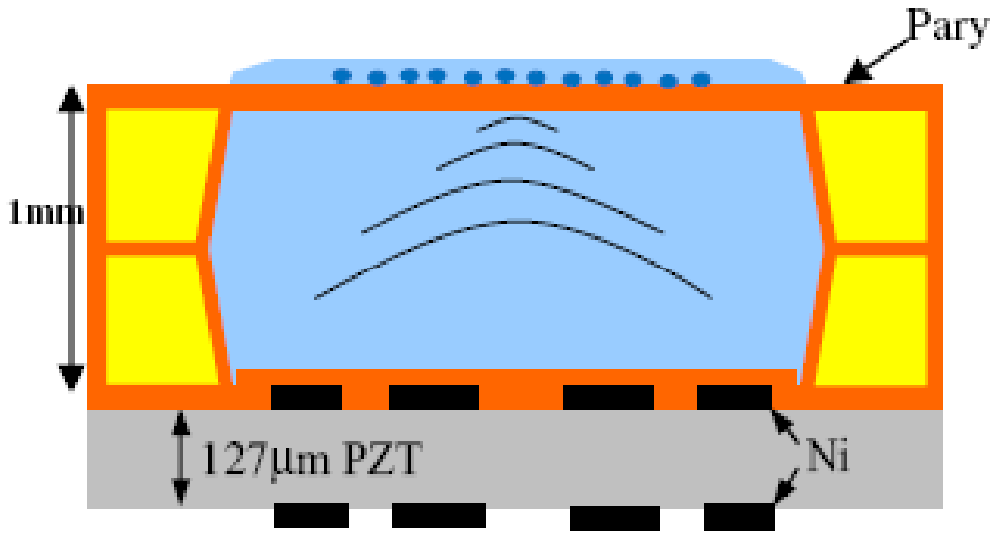
+ (b) deposit and pattern the first parylene layer as the lens material

+ (c) Remove the photoresist with acetone overnight,

+ (d) Deposit another 4~5 μm thick parylene to seal the release holes to complete the lens.

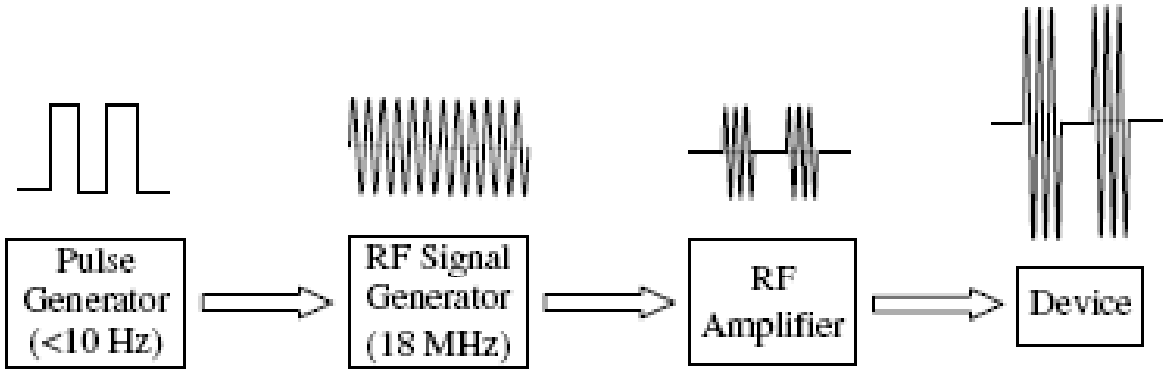
# BIO SAMPLE PREPARATION

- Chamber is fabricated with bulk micromachining using KOH anisotropic etching
- SFAT bonded with a chamber with cells growing on the top.
- A monolayer of the Bovine Aortic Endothelial Cells (BAECs)



# EXPERIMENT SETUP

- A RF system is set up to supply a burst of 18 MHz signals and a CCD video system is to capture the image of cavitation.
- The schematic of RF power supply system:
  - + 18 MHz RF signals are produced by the signal generator.
  - + RF signal is modulated and gated with a pulse signal and with a pulse repetition rate (PRR) of less than 10 Hz and a pulse width of 1ms.
  - + Then these signals are amplified to reach the voltage of Vp-p of 220V with RF amplifier.

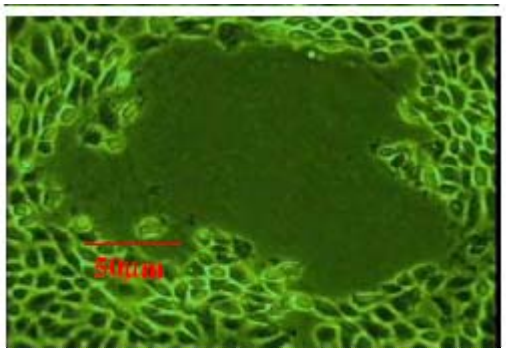


# Experimental results

- Acoustic waves are generated by the piezoelectric sheet, propagated into the culture media.
- Well focused acoustic waves produce air bubbles.
- Within 40 pulses, the cavitation breaks and detaches the cells at the focal point within the area of around 160 μm by 200 μm,

Air bubbles are produced

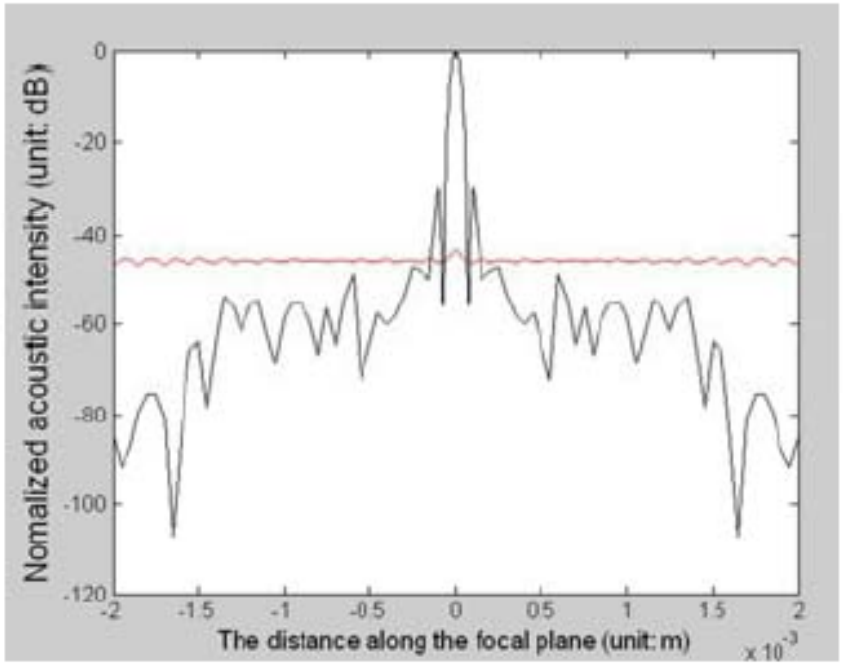
Cell lysis: Before

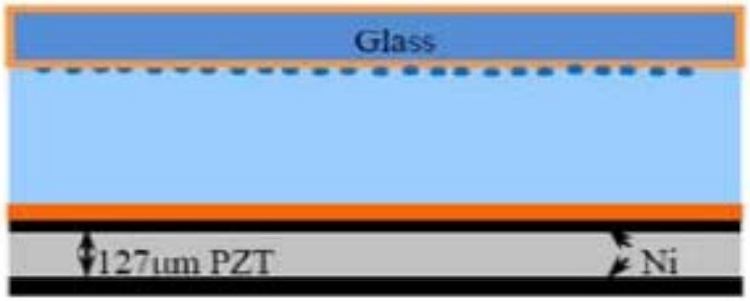


Cell lysis: After

# Focal effect of SFATs

- Un-patterned PZT transducer to produce uniform acoustic waves acting on BAECs
- To compare SFATs with transducers without such focal effect.

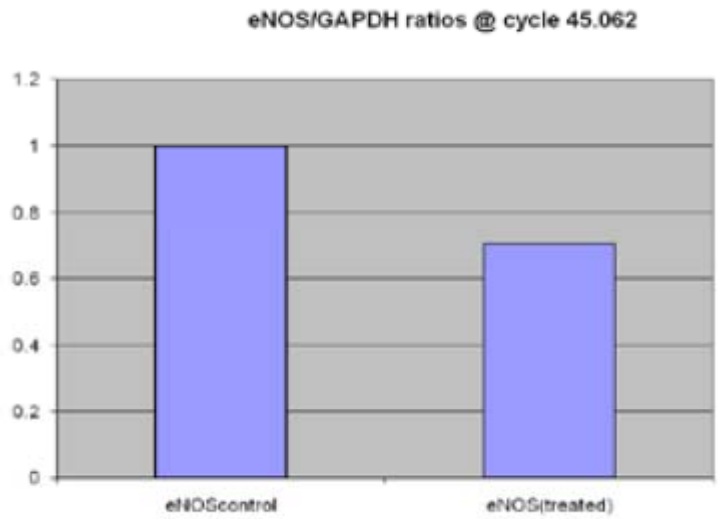



+ With SFAT (black)
+ unpatterned PZT (red).
+ The peak intensity at SFAT's focal point is 25W/cm2.

# Focal effect of SFATs

- Un-patterned transducer have no visible trace of cells being lysed and would only have moderate biological effects on the cells.
- SFAT would not harm the cells and produce a localized cell lysis on the focal spot where the coustic intensity is high.




+ *There is no lysis effect from SFAT on the cells outside focal area*

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- The SFAT working at 18 MHz is able to produce well-focused acoustic waves at the focal point, with acoustic intensity as high as 25 $W/cm^2$
- Such high intensity is beyond the threshold of the cavitation, and small bubbles have been observed.
- The heat and pressure have been shown to effectively lyse cells through detachment of cells from the focused spot.
- Would be ideal to for localized cell lysis and potentially tumor treatment.

# Reference


- [1] J. Zhu, X. Qiu, J. Oiler, C. Yu, Z. Wang, C. Lee, T.K. Hsiai, E. S. Kim, and H. Yu, “LOCALIZED CELL LYSIS BY SELF FOCUSED ACOUSTIC TRANSDUCERS,” *Transducers 2009*, Denver, CO, USA, June 21-25, 2009, pp. 609-611

- [2] Hongyu Yu and Eun Sok Kim, “ULTRASONIC UNDERWATER THRUSTER,” *IEEE Intl. Conference of Micro Electro Mechanical Systems*, Sorrento, 2004, pp. 486-489

- [3] Jae Wan Kwon, Hongyu Yu, Qiang Zou and Eun Sok Kim, “Directional droplet ejection by nozzleless acoustic ejectors built on ZnO and PZT,” *J. Micromech. Microeng*,” Vol.16, 2006, pp. 2697-2704

- [4] Chuang-Yuan Lee, Hongyu Yu and Eun Sok Kim, “ACOUSTIC EJECTOR WITH NOVEL LENS EMPLOYING AIR-REFLECTORS,” *IEEE Intl. Conference of Micro Electro Mechanical Systems*, Sorrento, Istanbul, Turkey, January 22 - 26, 2006, pp. 170-173

*Thanks for your attention!!*