IEEE Ultrasonics, Ferroelectrics, and Frequency Control Society

Acoustic Tweezing: Modelling, Implementation and Applications

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IEEE International Ultrasonics Symposium
Prague, Czech Republic

21 July 2013

Course Content

The acoustic radiation force

(Charles Courtney, University of Bath)

Tweezing with planar resonators

(Martyn Hill, University of Southampton)

Dexterous acoustic tweezing

(Bruce Drinkwater, University of Bristol)

How to make an acoustic tweezer

(Sandy Cochran, University of Dundee)

Applications of acoustics tweezers

(Martyn Hill, University of Southampton)

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The acoustic radiation force

(Hand-out to follow)

Dr Charles Courtney
University of Bath, UK

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Applications of acoustics tweezers

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Dexterous Acoustic Tweezing

Professor Bruce Drinkwater
University of Bristol, UK

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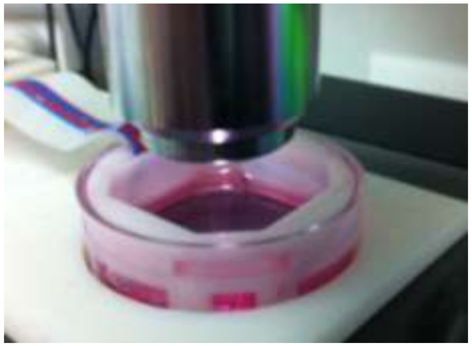
Contents

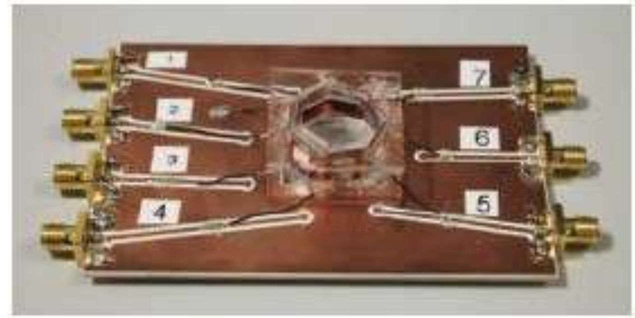
- Introduction to array-based tweezing
- Effect of device boundaries
- Design and modelling of dexterous devices
- High frequency beam-based tweezing
- Current capabilities and future directions

Examples of array devices

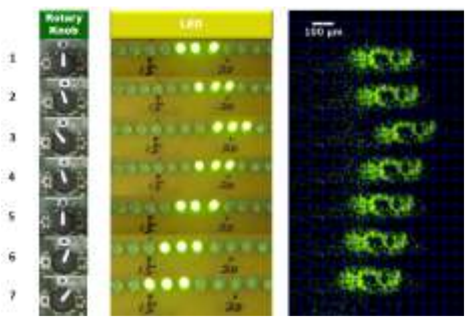
- 4-transducer water-backed[1]



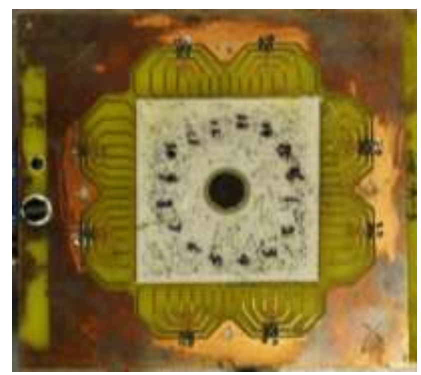
- Heptagon[2]



- Planar array[3]

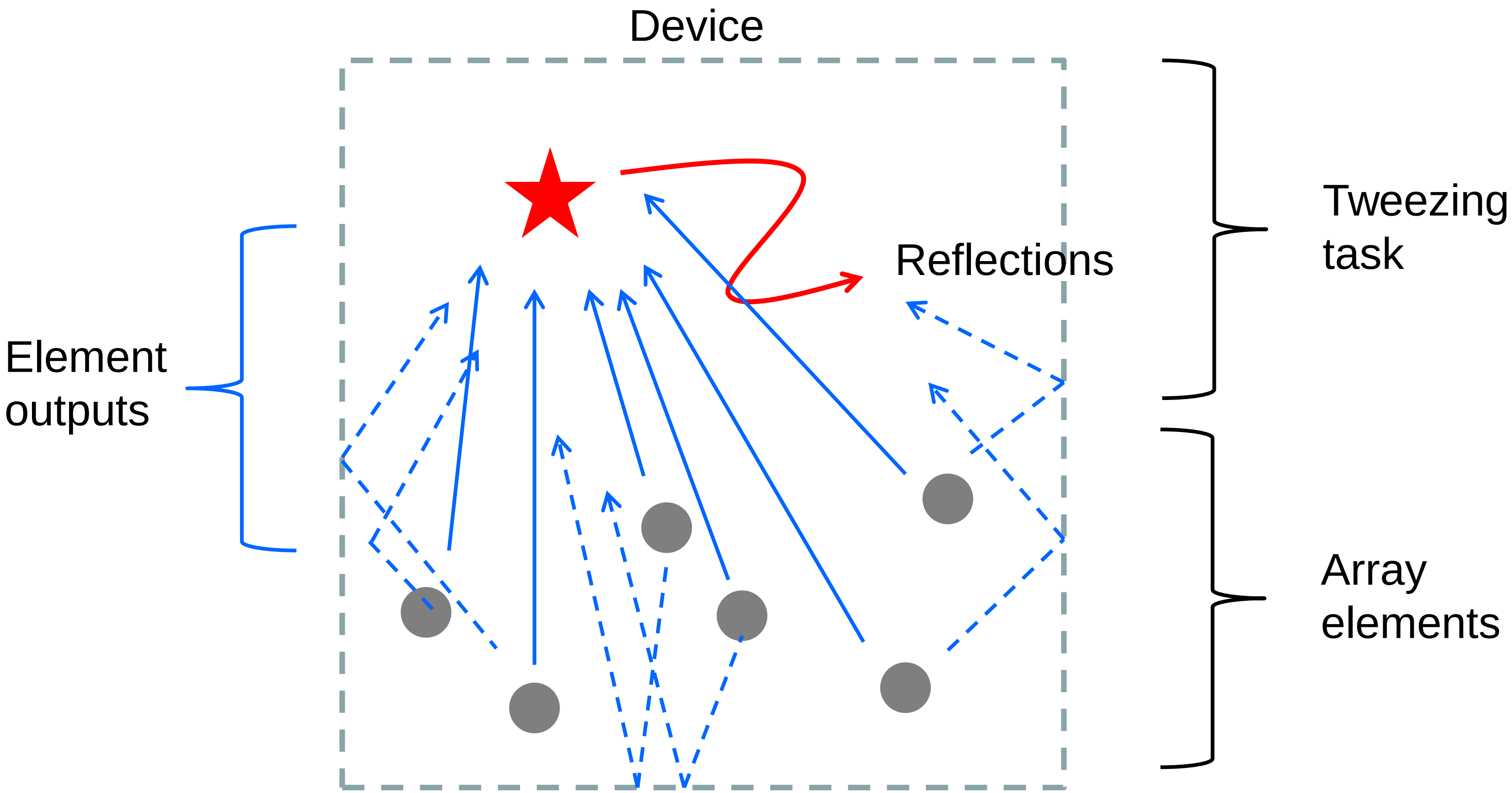


- Circular array[4]



[1]Courtney et al in APL 101 (23), 2012
[2]Bernassau et al in IEEE UFFC 58(10), 2011
[3]Glynne-Jones et al in IEEE UFFC 59(6), 2012
[4]Courtney et al in APL 102 (12), 2013

Array-based manipulation

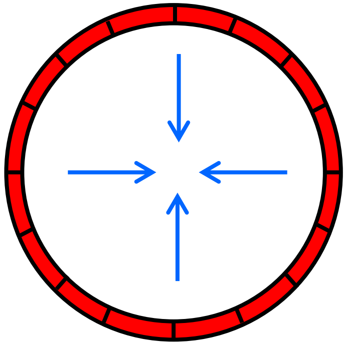


Questions

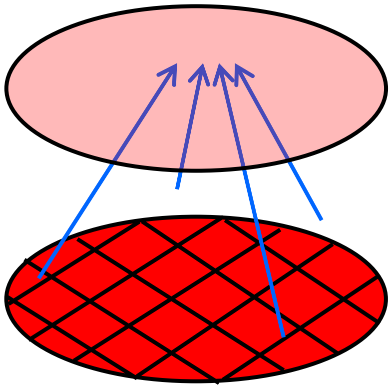
- How to arrange the array elements?
- What acoustic field is needed to complete the tweezing task?
- How can this required acoustic field be created?
- What is the influence of the device boundaries?

Current devices

- Surround the region with elements for in-plane tweezing



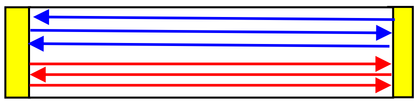
- Use a plane of elements to create a beam for out-of-plane tweezing



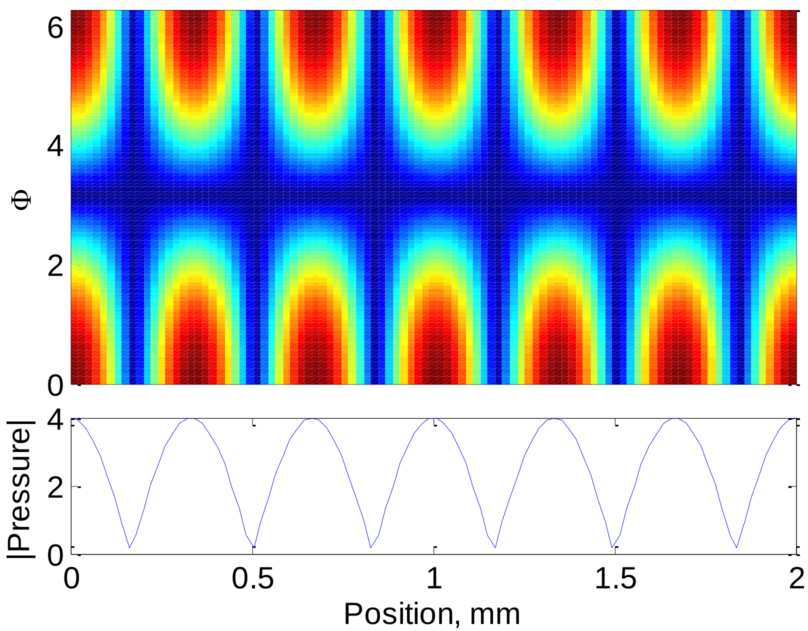
These concepts could be merged for 3D manipulation

Effect of boundaries

Reflective boundaries

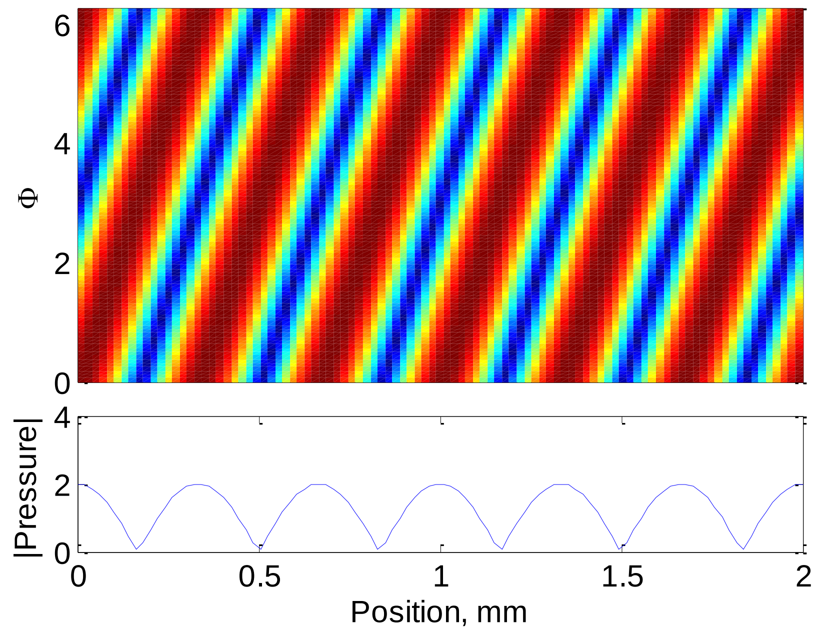


$u(x)$= 2A[cos(kx)+$e^{i\phi/2}$cos(kx)]

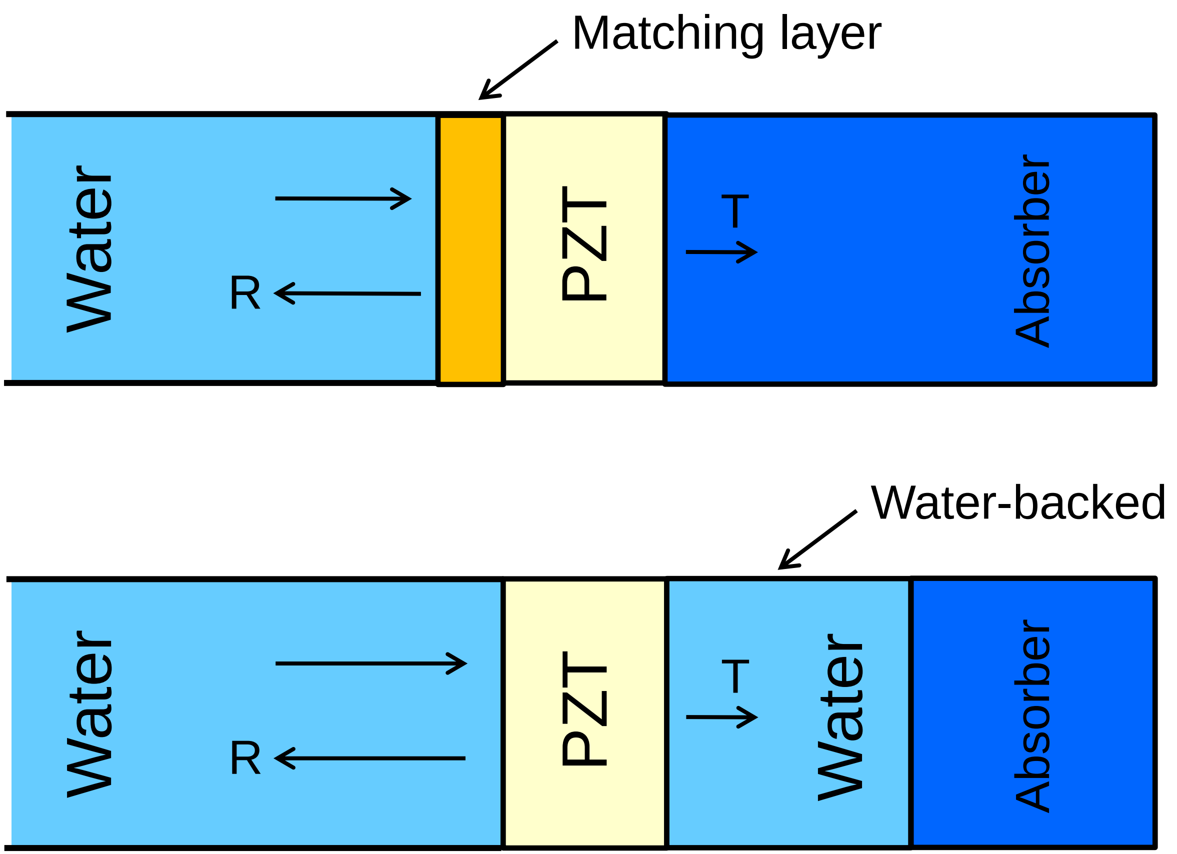


Transparent boundaries

$u(x)$=A[e^{ikx}+ $e^{-i(kx-\phi)}$]



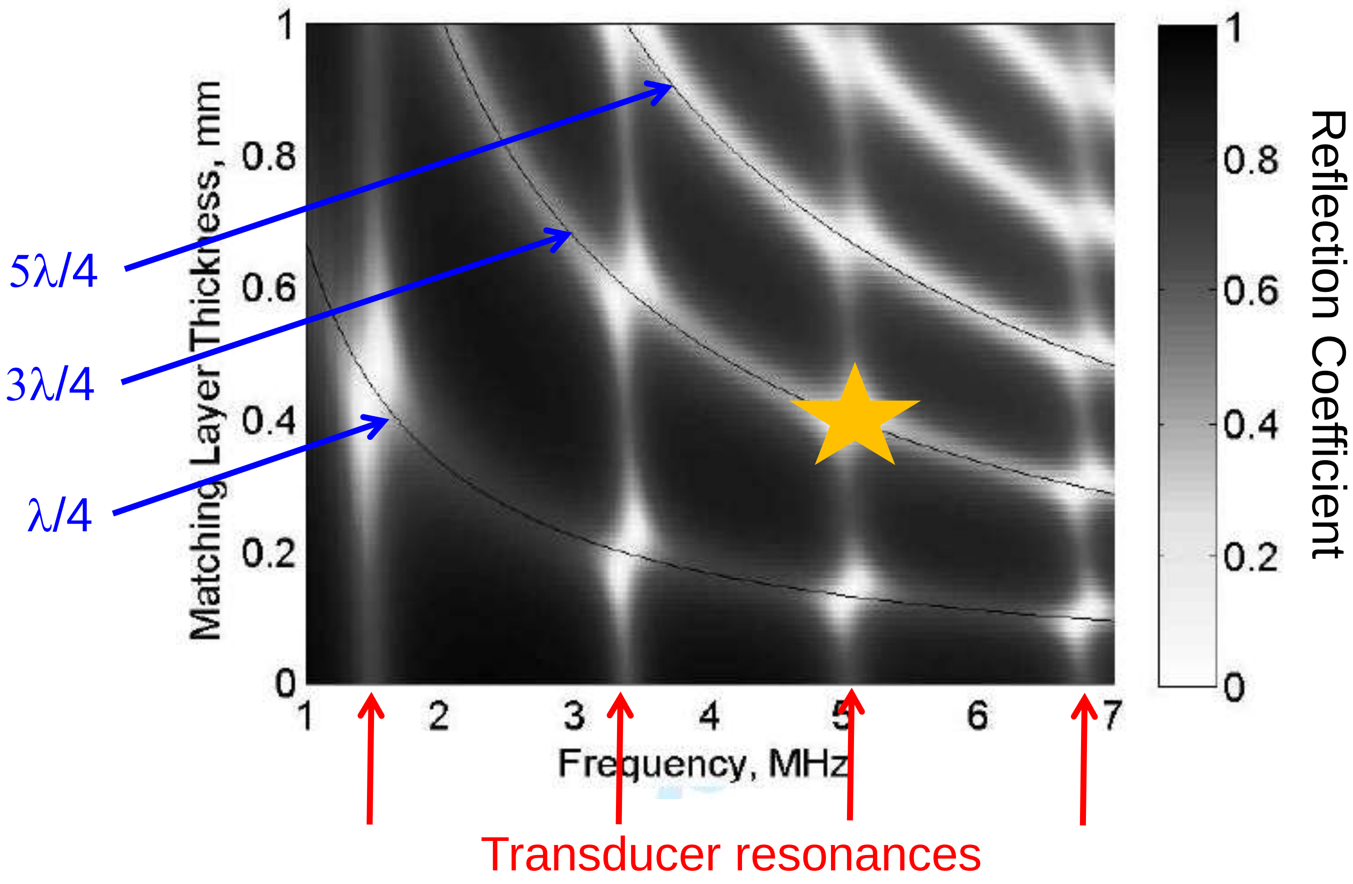
Transparent boundaries



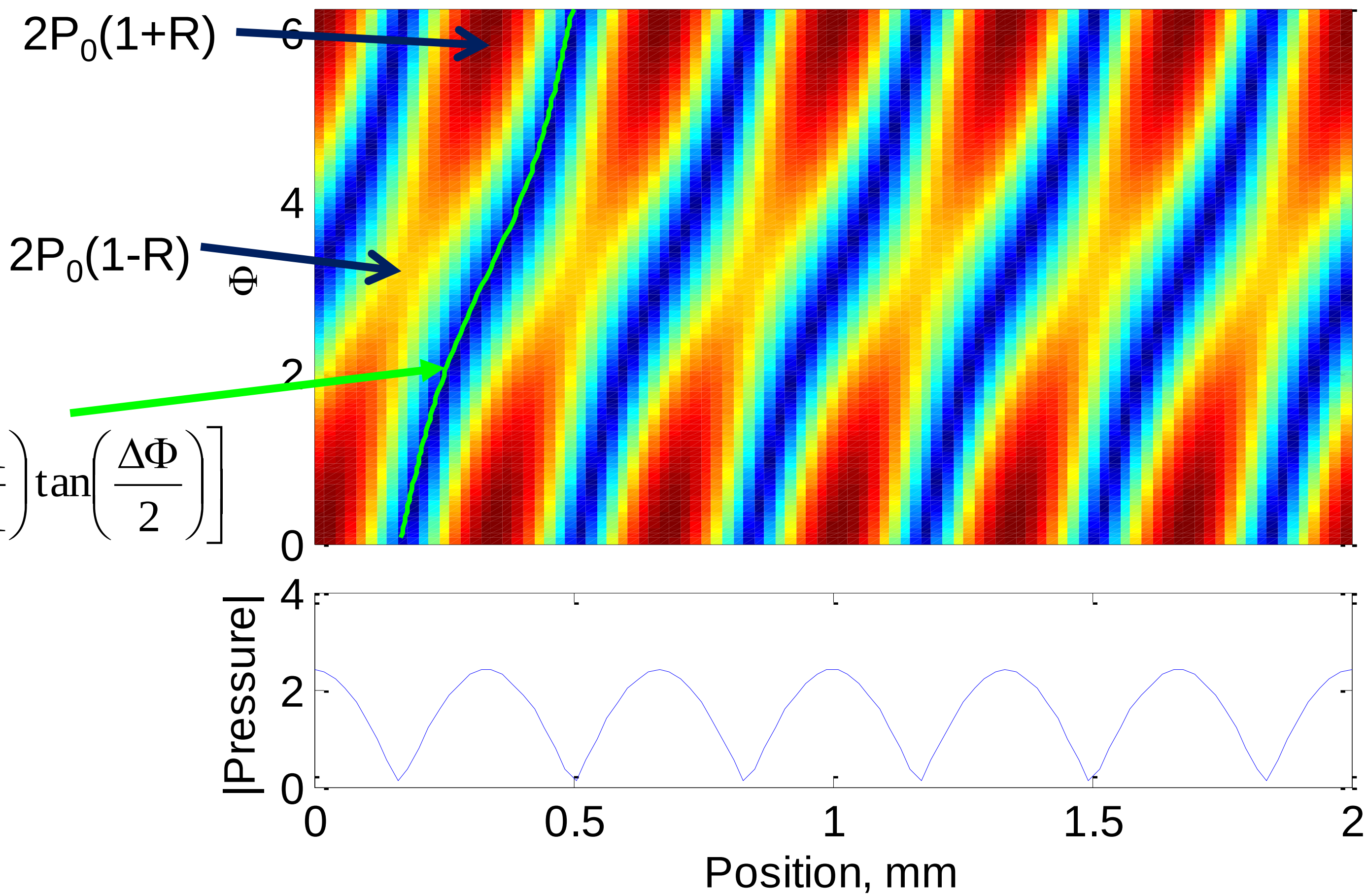
Grinenko et al in APL 101(23), 2012

Transparent boundaries

- Matching layer design

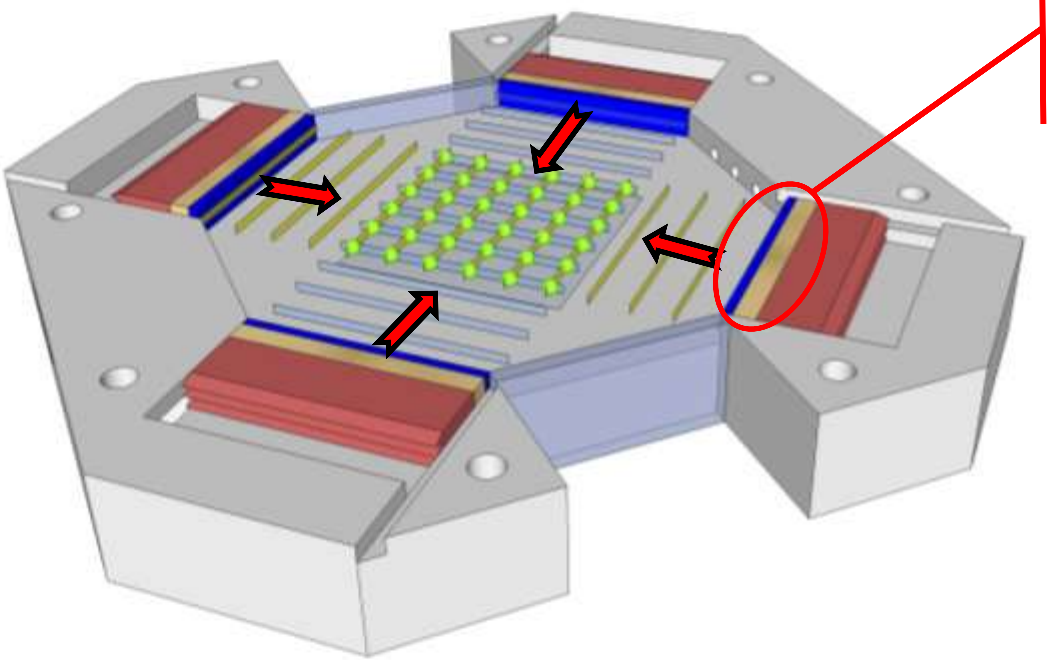


Effect of partial reflection



$$\Delta x = \frac{1}{k}\arctan\left[\left(\frac{R-1}{R+1}\right)\tan\left(\frac{\Delta\Phi}{2}\right)\right]$$

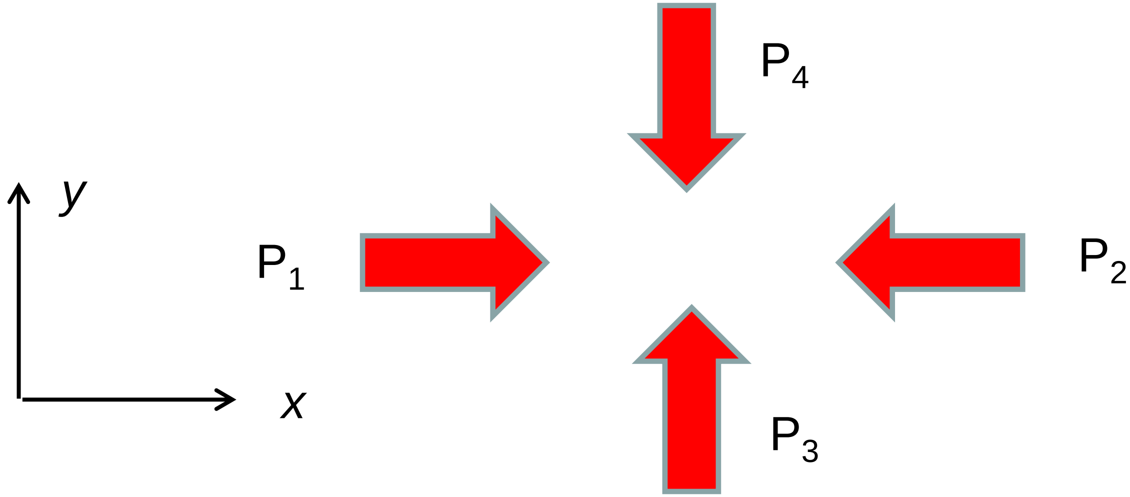
4-element array



- Rectangular grid pattern formed
- Grid can be translated in the plane of the device
- Applications in biology and materials

Courtney et al in Proc Roy Soc 468, 2012

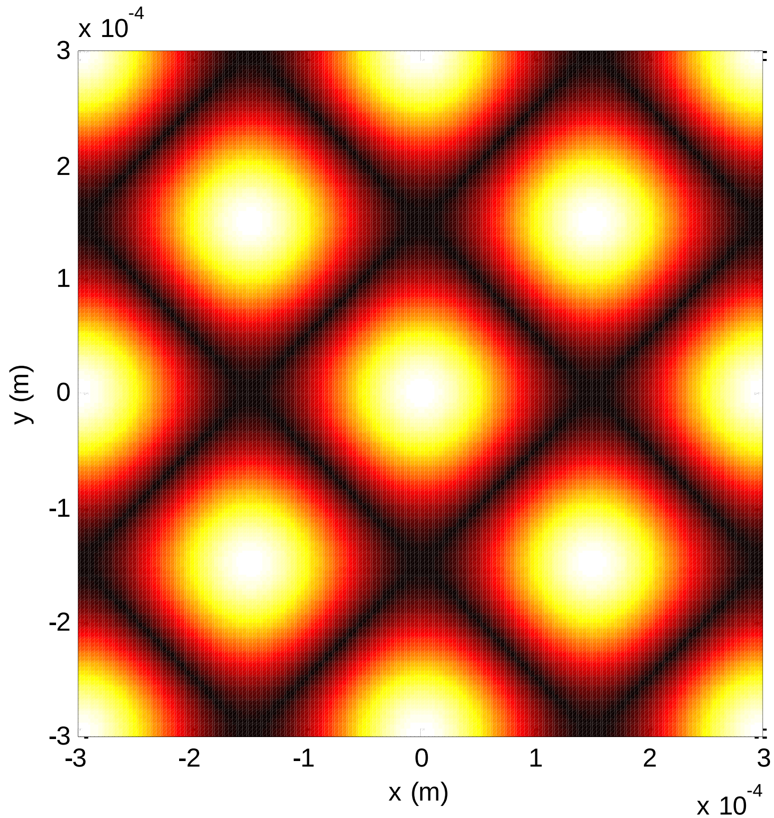
Simulating the device



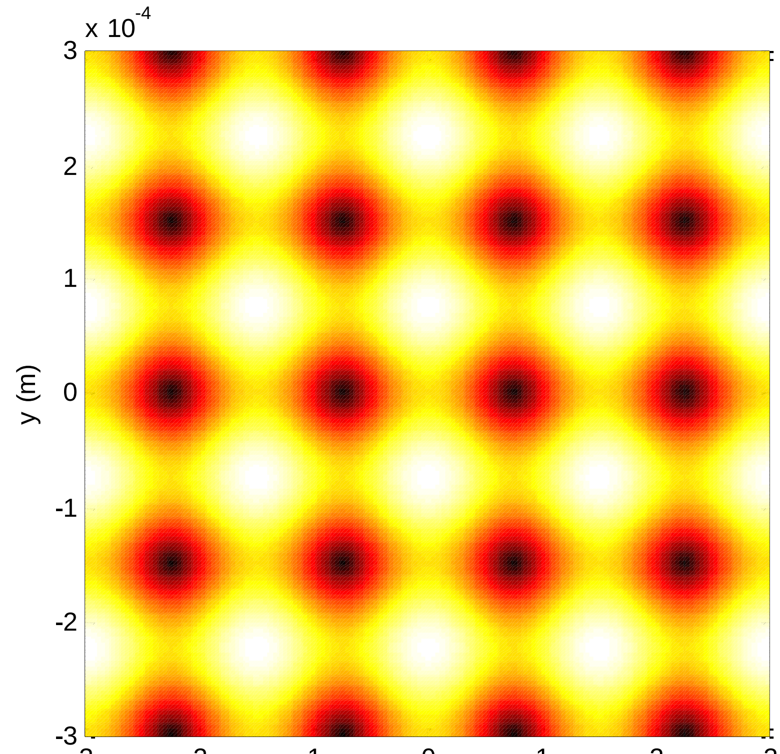
$$
\left.
\begin{aligned}
P_1(x,y) &= P_0 \exp[i(kx + \varphi_1)] \\
P_2(x,y) &= P_0 \exp[i(-kx + \varphi_2)] \\
P_3(x,y) &= P_0 \exp[i(ky + \varphi_3)] \\
P_4(x,y) &= P_0 \exp[i(-ky + \varphi_4)]
\end{aligned}
\right\}
$$

4 plane waves, no reflections

Acoustic Pressure



$$\phi_y = \phi_x$$

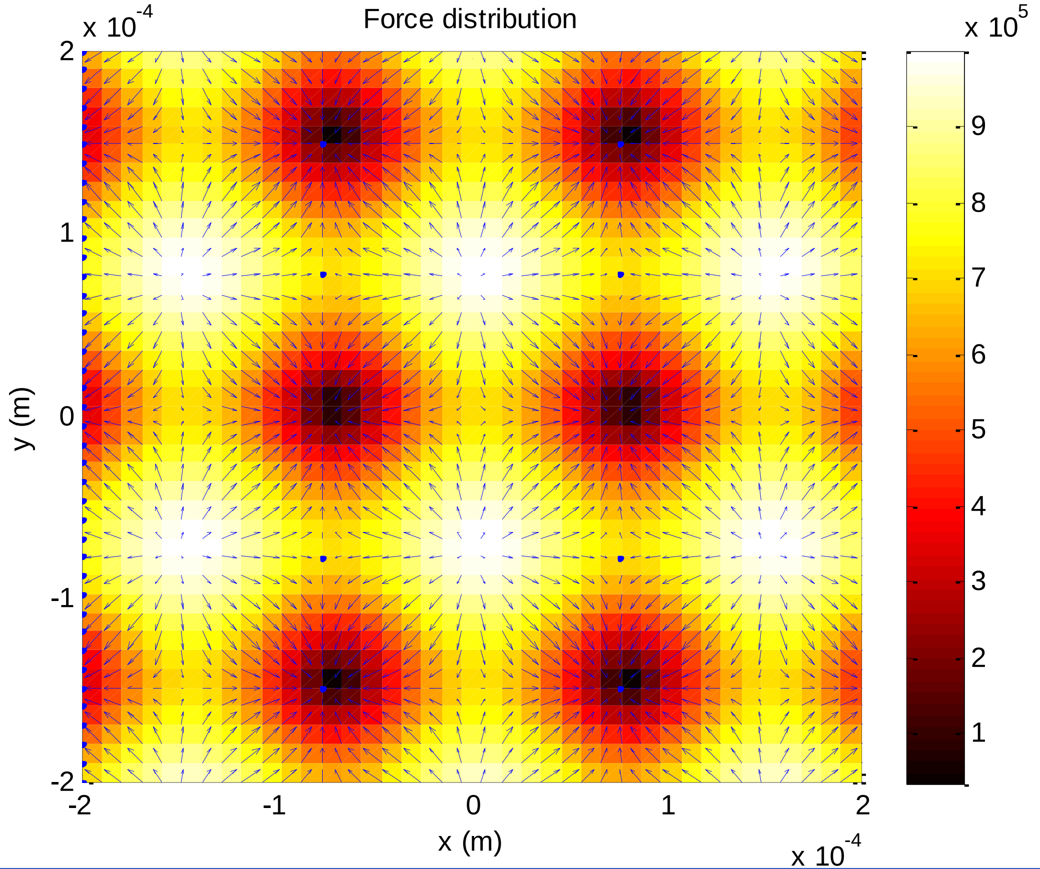


$$\phi_y = \phi_x + \frac{\pi}{2}$$

Where, $\varphi_x = \frac{\varphi_1+\varphi_2}{2}$, and $\varphi_y = \frac{\varphi_3+\varphi_4}{2}$

Acoustic radiation force

- Using Gor'kov $U = 2\pi a^3 \rho \left\{ \frac{\overline{P^2}}{3\rho^2 c^2} f_1 - \frac{\overline{v^2}}{2} f_2 \right\}$
- $f_1 = 1 - \frac{K}{K_0}$
- $f_2 = 2\frac{\rho_0 - \rho}{2\rho_0 + \rho}$

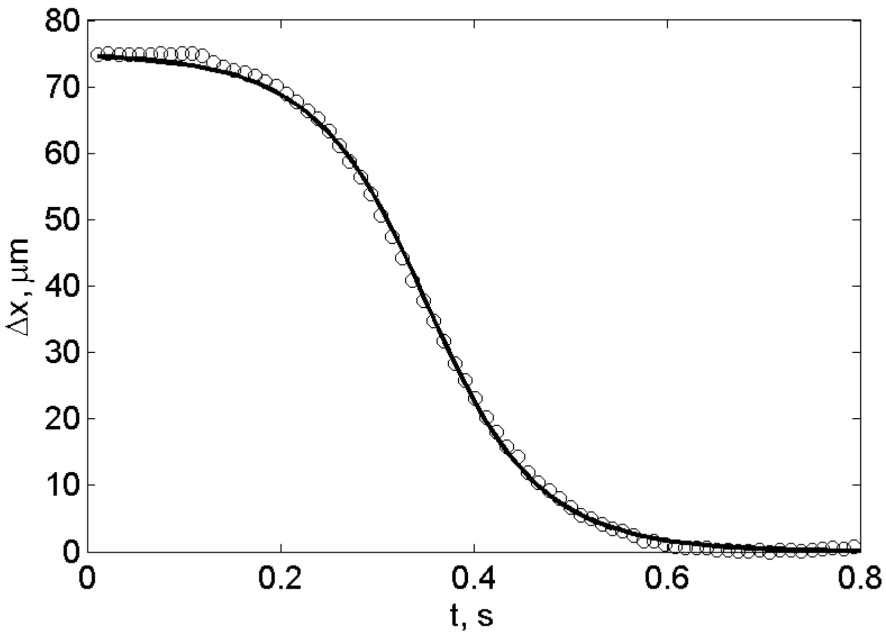


And then

- $F = -\nabla U$

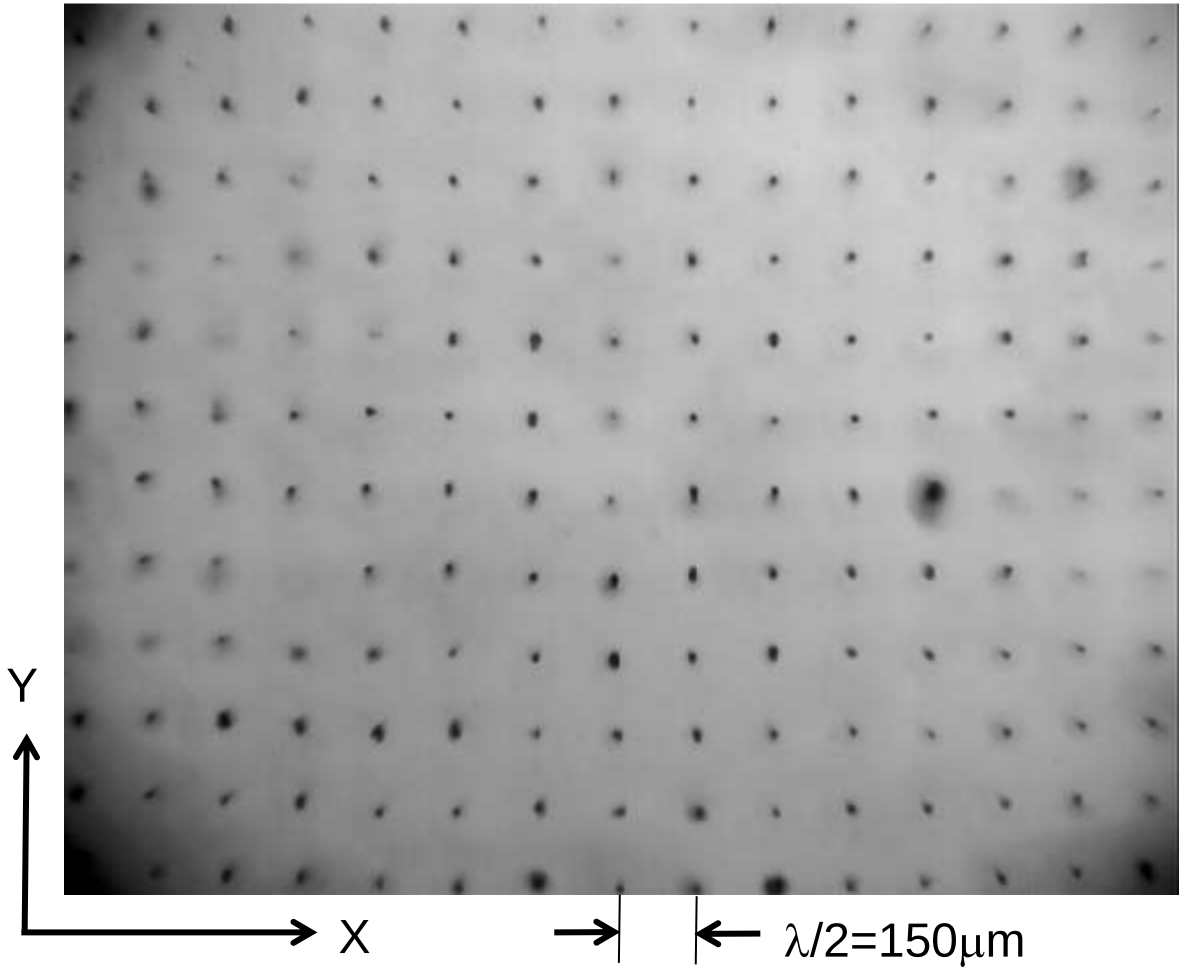
Force Measurement

- Locate single particle in trap.
- Shift acoustic field by λ / 2.
- Track motion with 200 fps camera.
- Fit solution for particle in sinusoidal potential well in presence of Stoke's drag



F_0=30 pN

10,000 trapping points

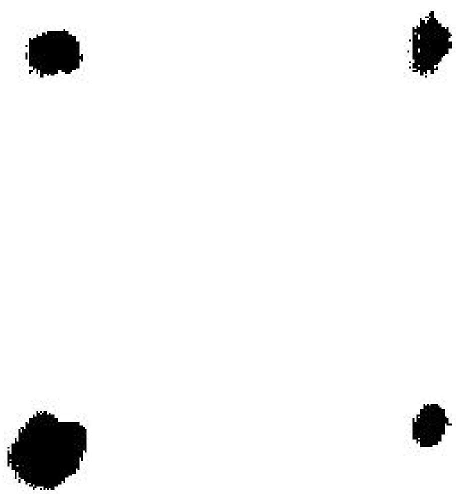


- Uniform grid of equal traps
- Translatable in X and Y

10μm diameter polystyrene spheres in water, 5MHz

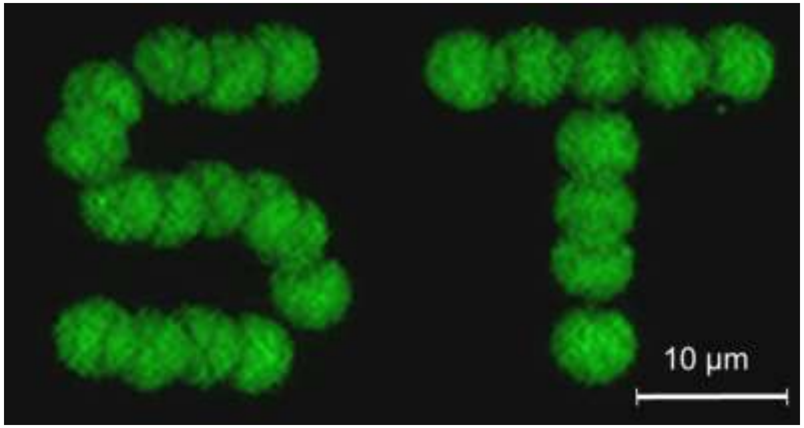
Translation of the acoustic field

Video



Four 10 µm particles

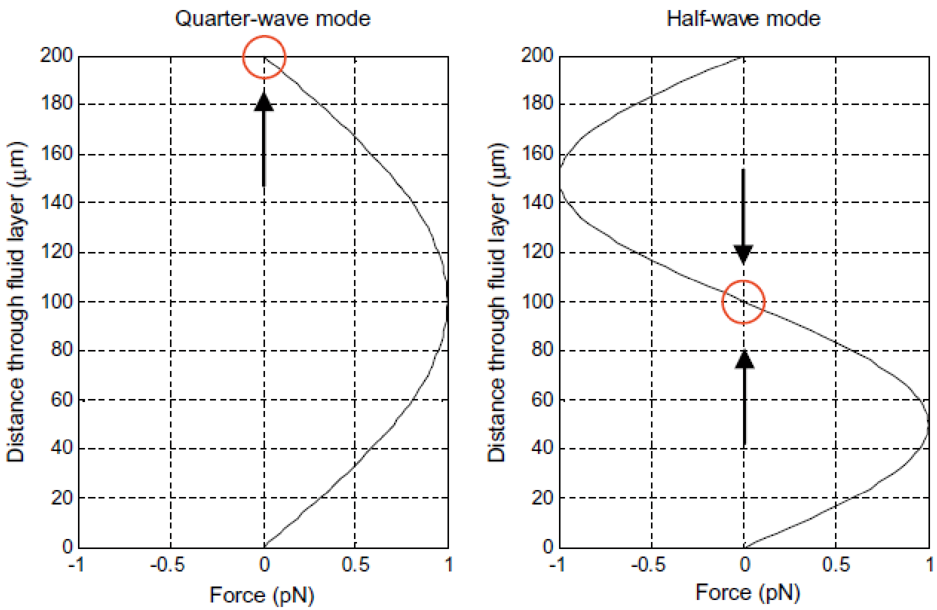
Composite photo



Composite image of a single 6 µm fluorescent particle maneuvered to shape the letters ‘ST’

Alternative concepts

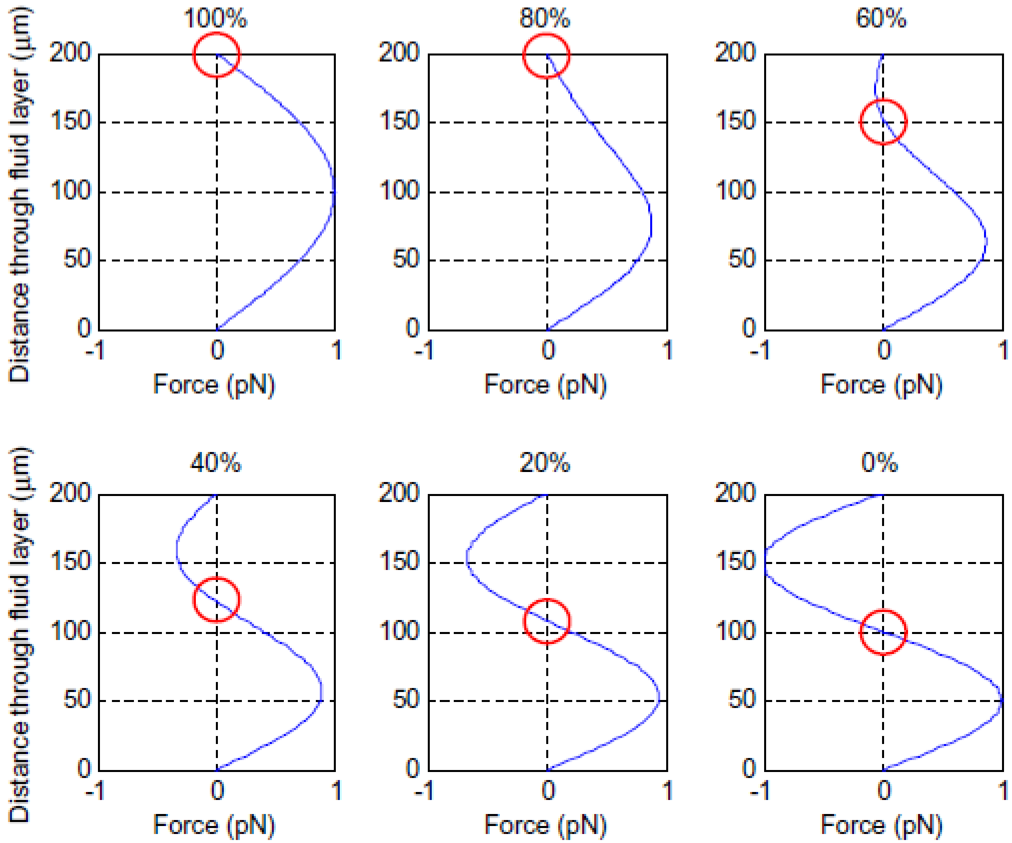
- Mode switching

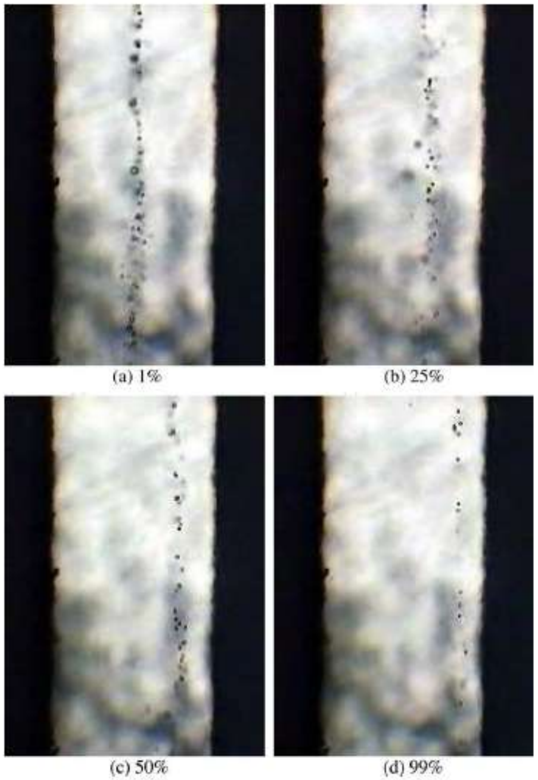


- $F_{Total} = qF_Q + (1 - q)F_H$

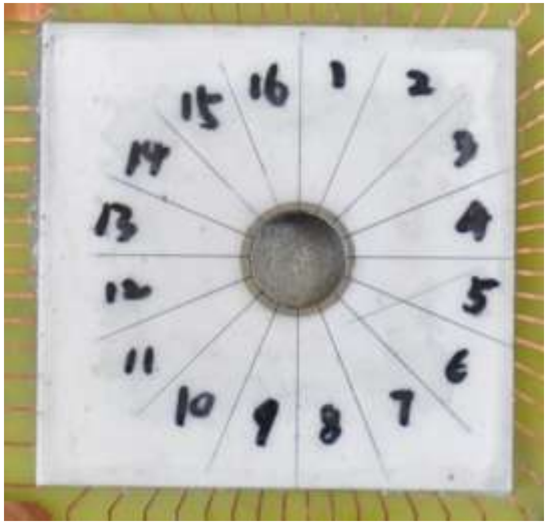
Mode switching

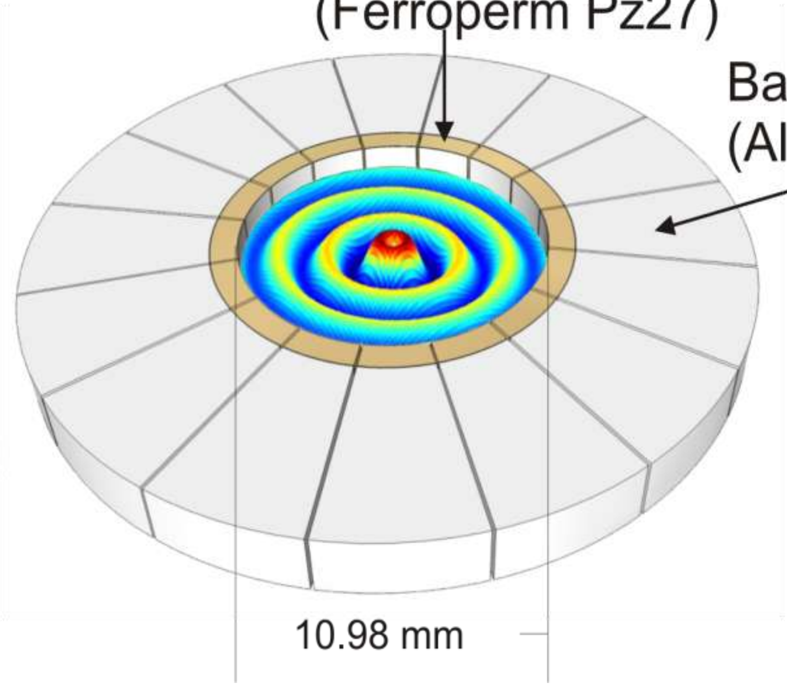
Varying the fraction of the quarter wavelength mode





Circular Array Device

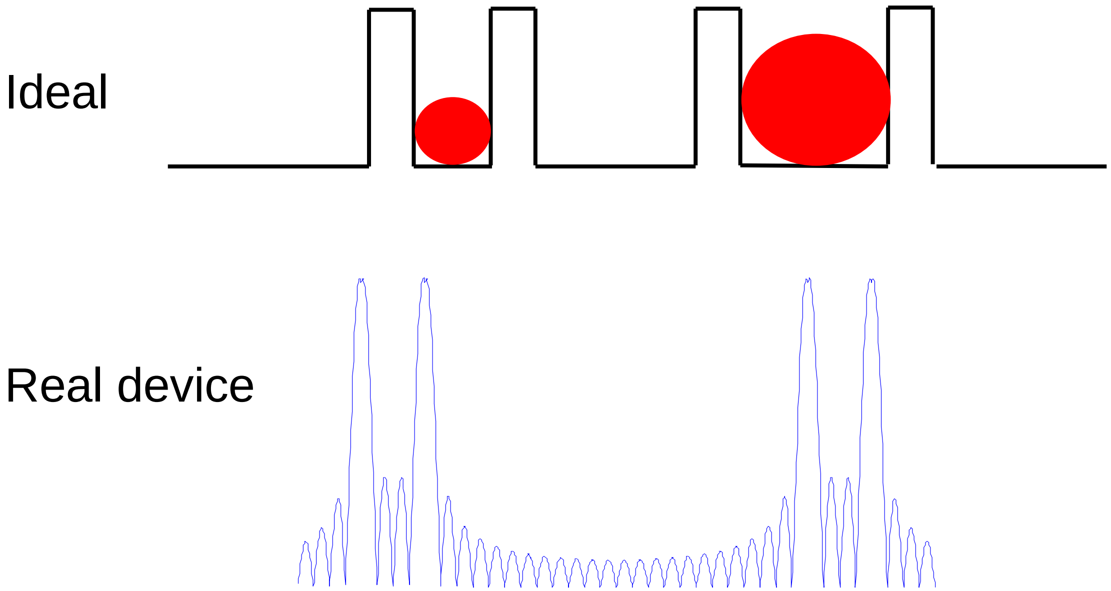




Courtney et al in APL 102(12), 2013

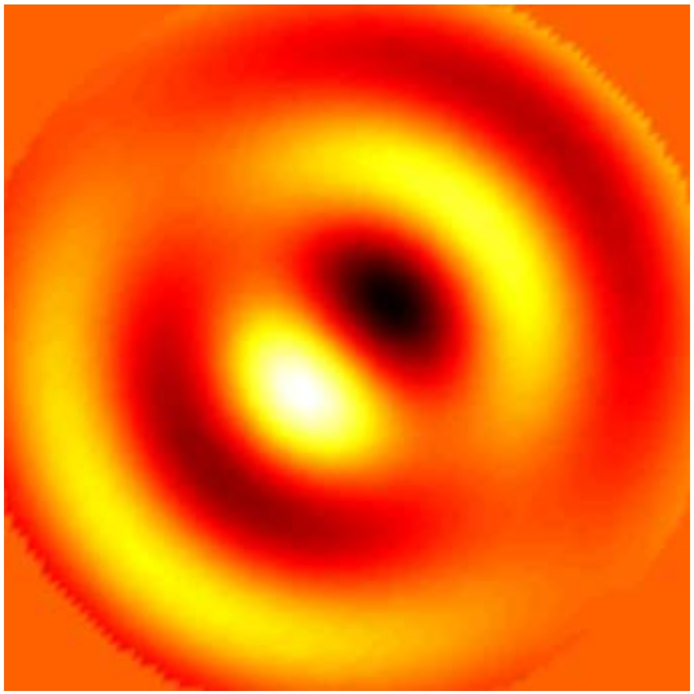
Ideal acoustic pressure field?

- Arbitrary trap locations
- Arbitrary trap numbers
- Sharp spatial gradients
- Minimal interference between traps

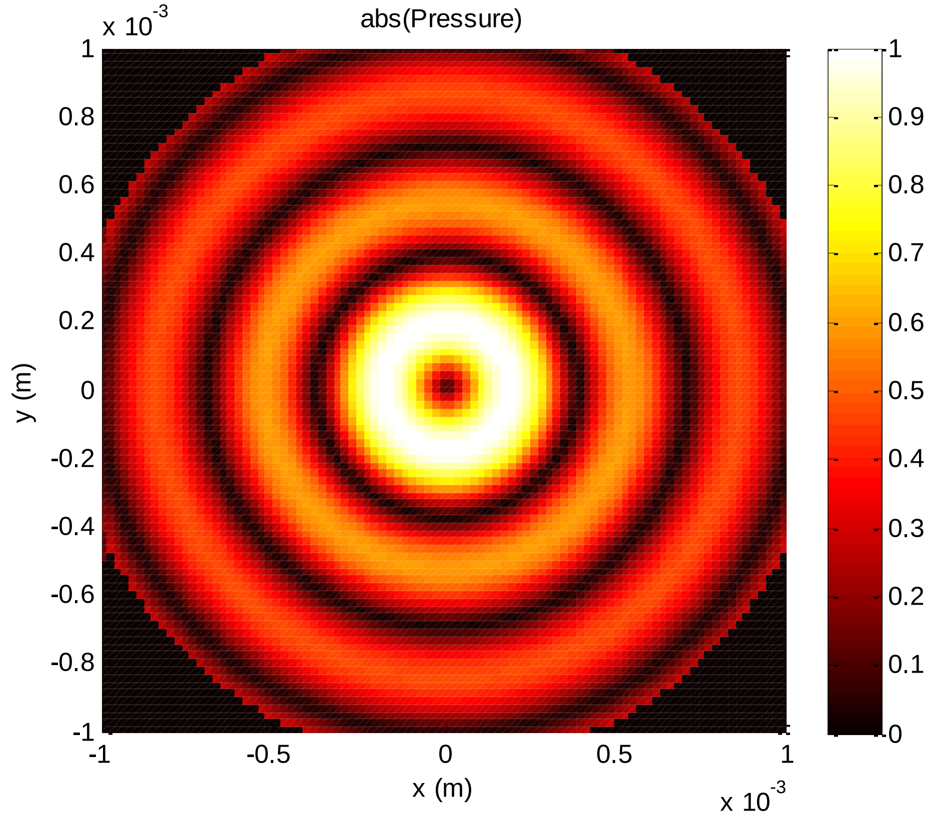


Helical* beam creates local minima

Instantaneous pressure (α=1)

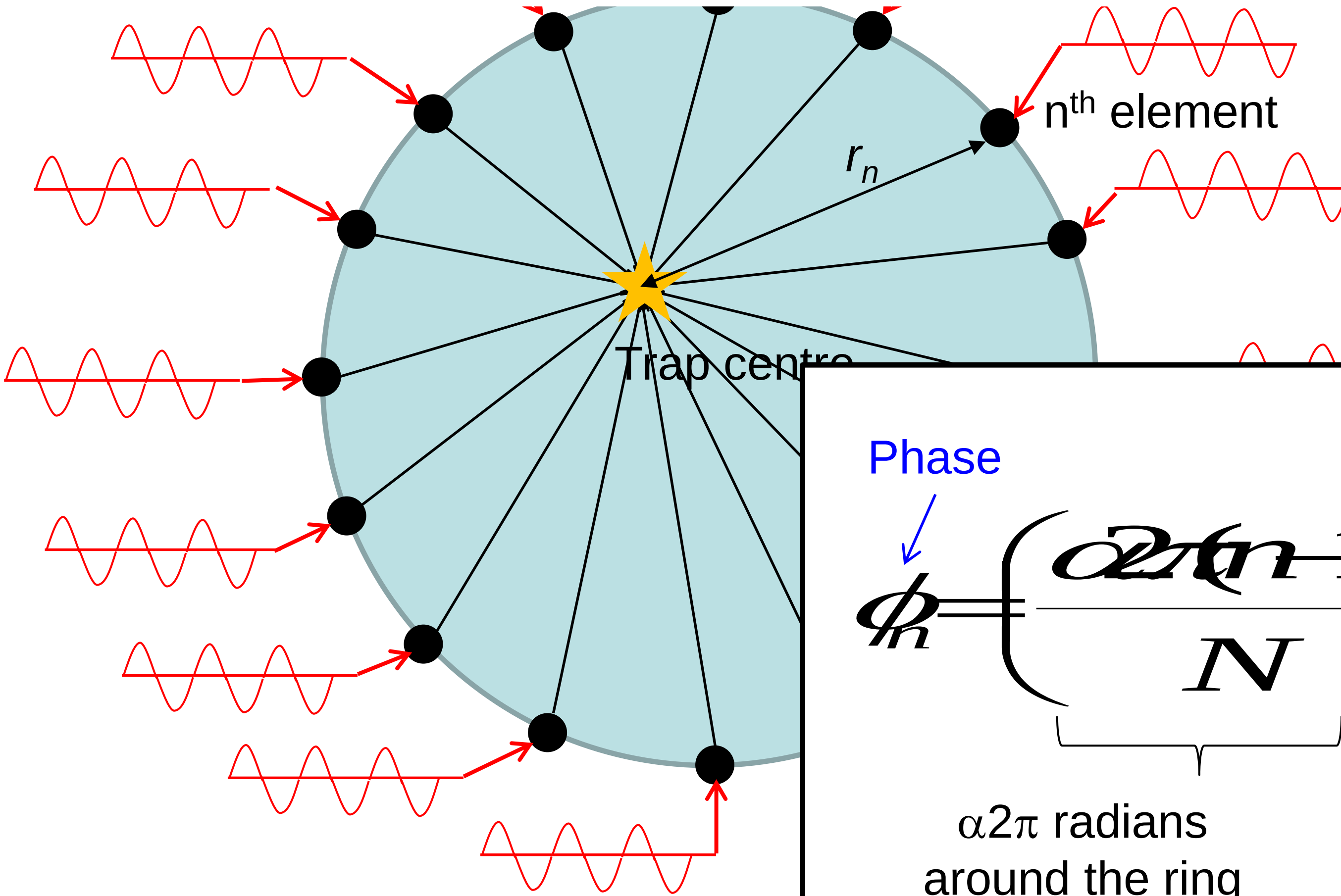


α=topological charge



*As used in optical tweezers, e.g. Grier, Nature 424, 2003

How to generate a Helical beam



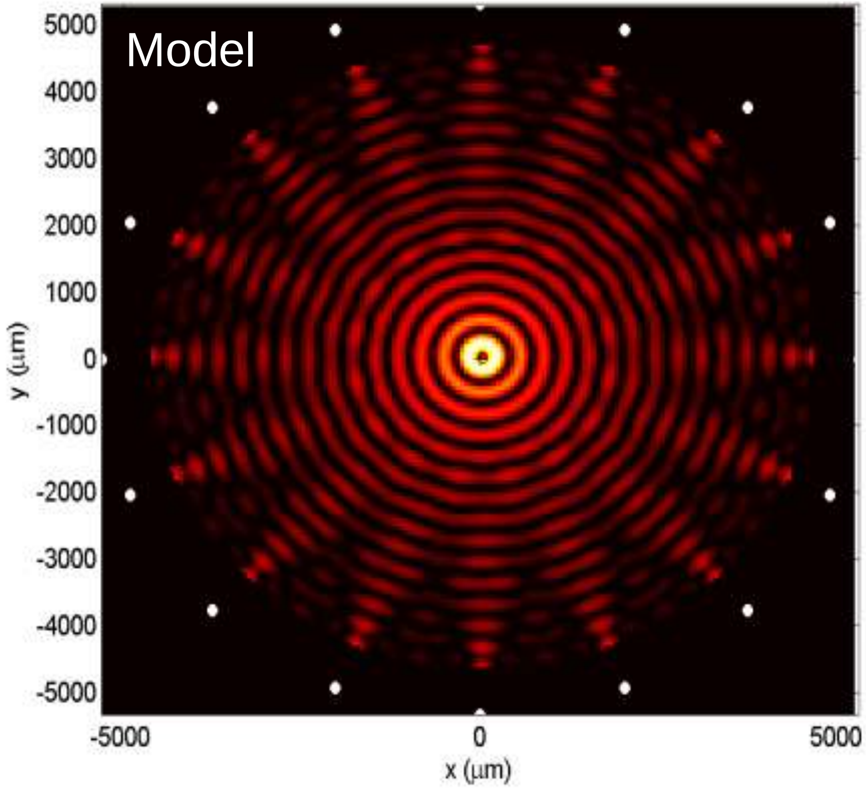
Phase

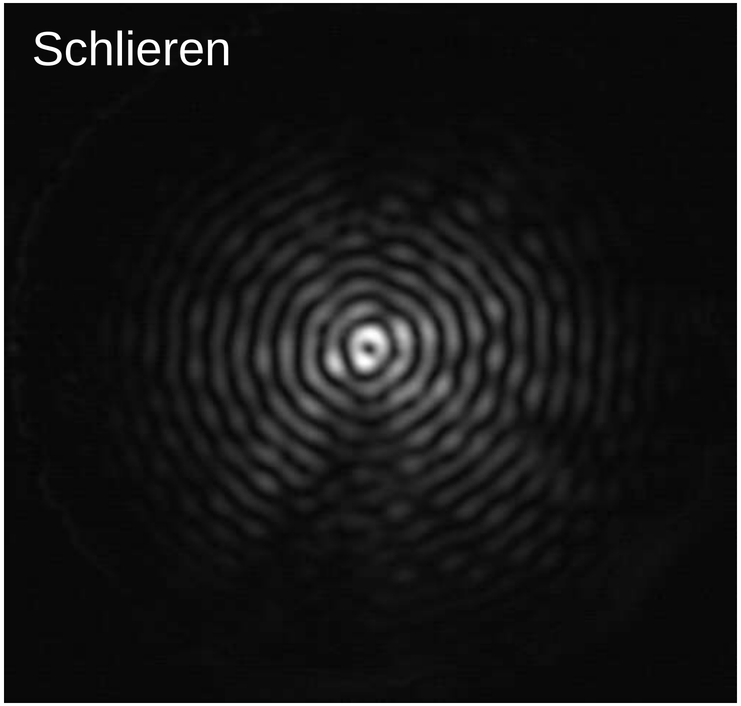
$$\phi_n = \left(\frac{\alpha 2\pi (n-1)}{N} - k r_n \right)$$

$\alpha 2\pi$ radians around the ring

Moves trap centre

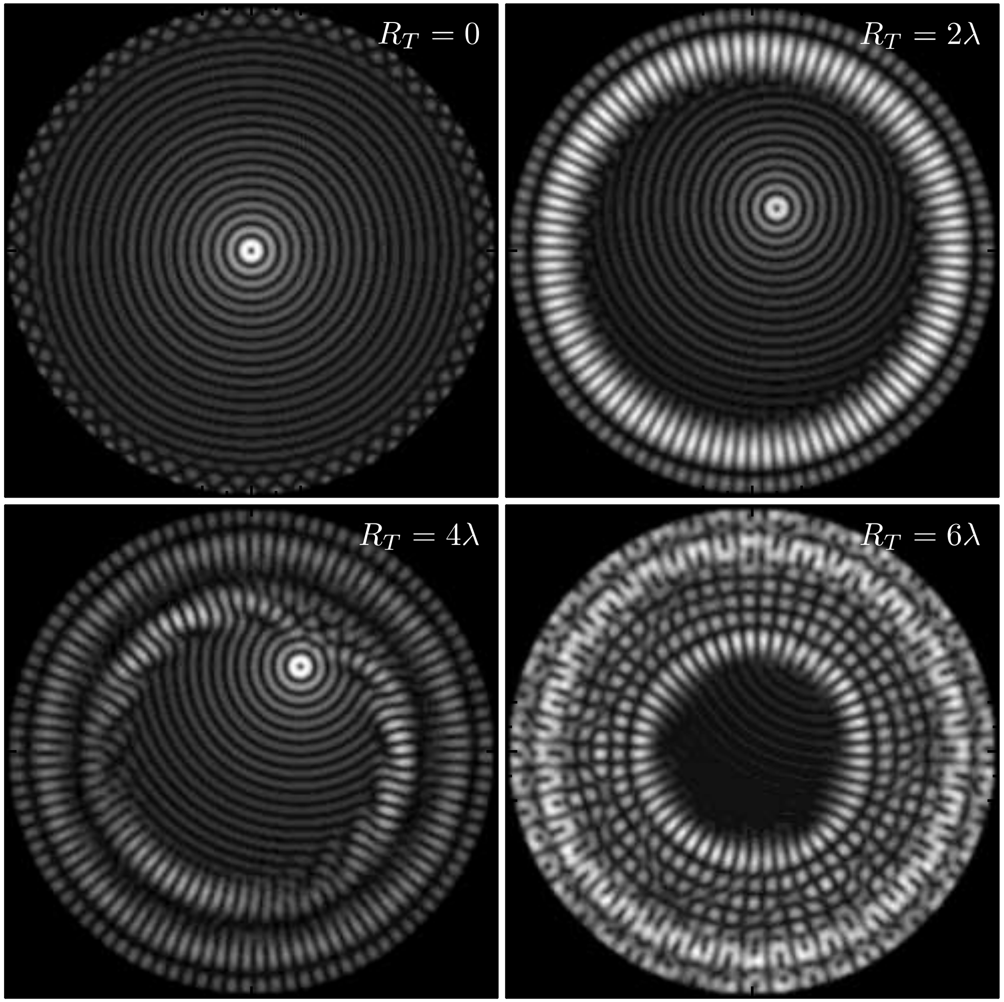
Effect of the number of elements





Performance limits and aliasing

N=60



- If the boundary is discretized, then, according to sampling theorem an inevitable aliasing appears

Target field

Artefact field

$$p(\boldsymbol{r}) = \underbrace{p_0 J_\alpha(kR_T)e^{i\alpha\theta_T}}_{\text{Target field}} + \underbrace{p'(\boldsymbol{r})}_{\text{Artefact field}}$$

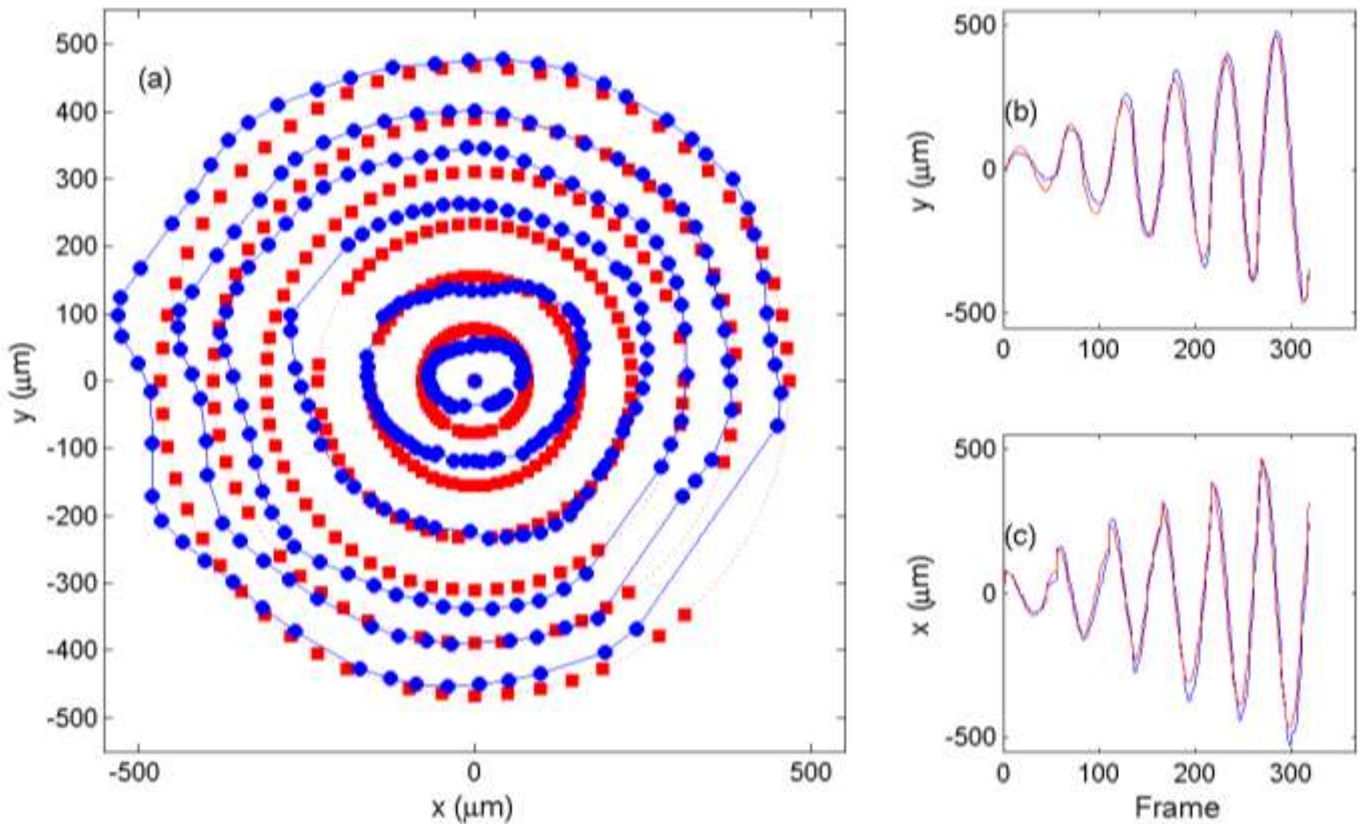
- Controllable area is defined by:

$$R_{T(Max)} = \frac{1}{2}\frac{(N-\alpha)}{\pi e}\lambda$$

$$\approx \frac{N\lambda}{17.08}$$

Grinenko et al in Proc. Roy Soc. 468, 2012

Particle positioning



Multiple traps

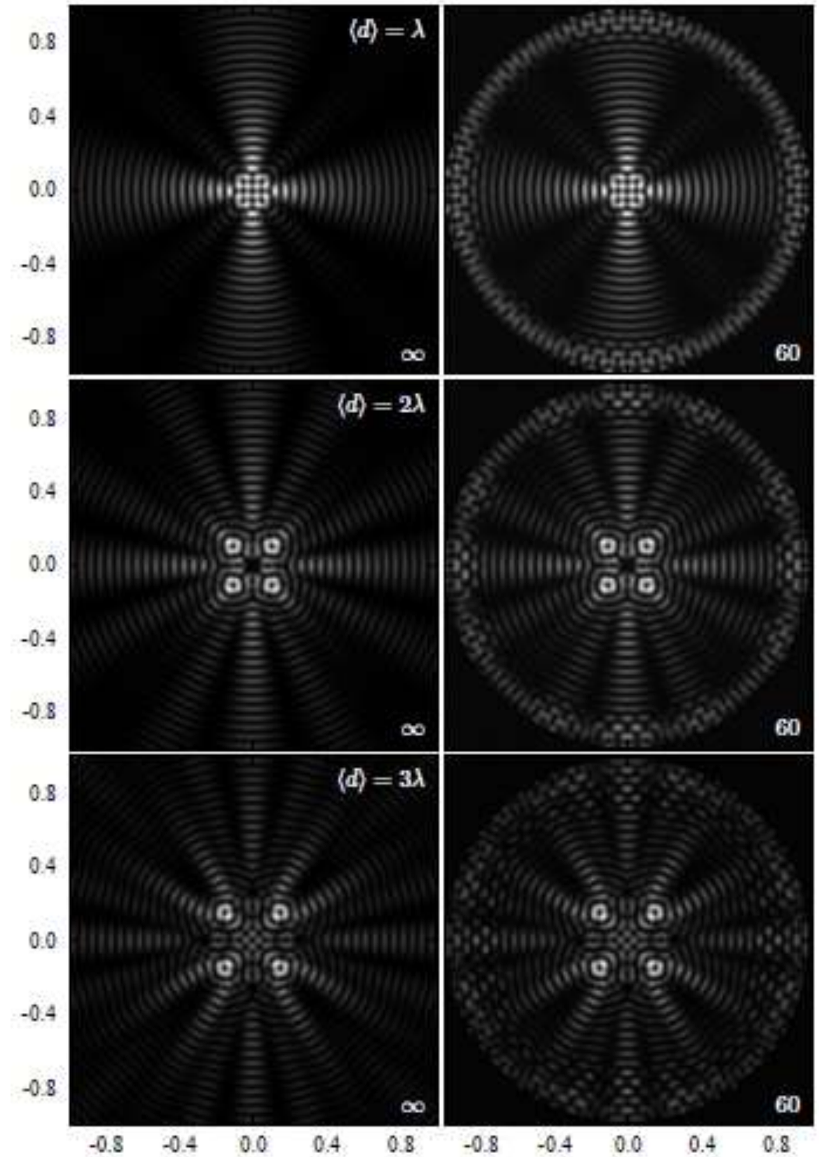
- n^{th} element and m^{th} trap

$$\phi_{nm} = \left(\frac{2\pi(n-1)}{N} - kr_{nm} \right)$$

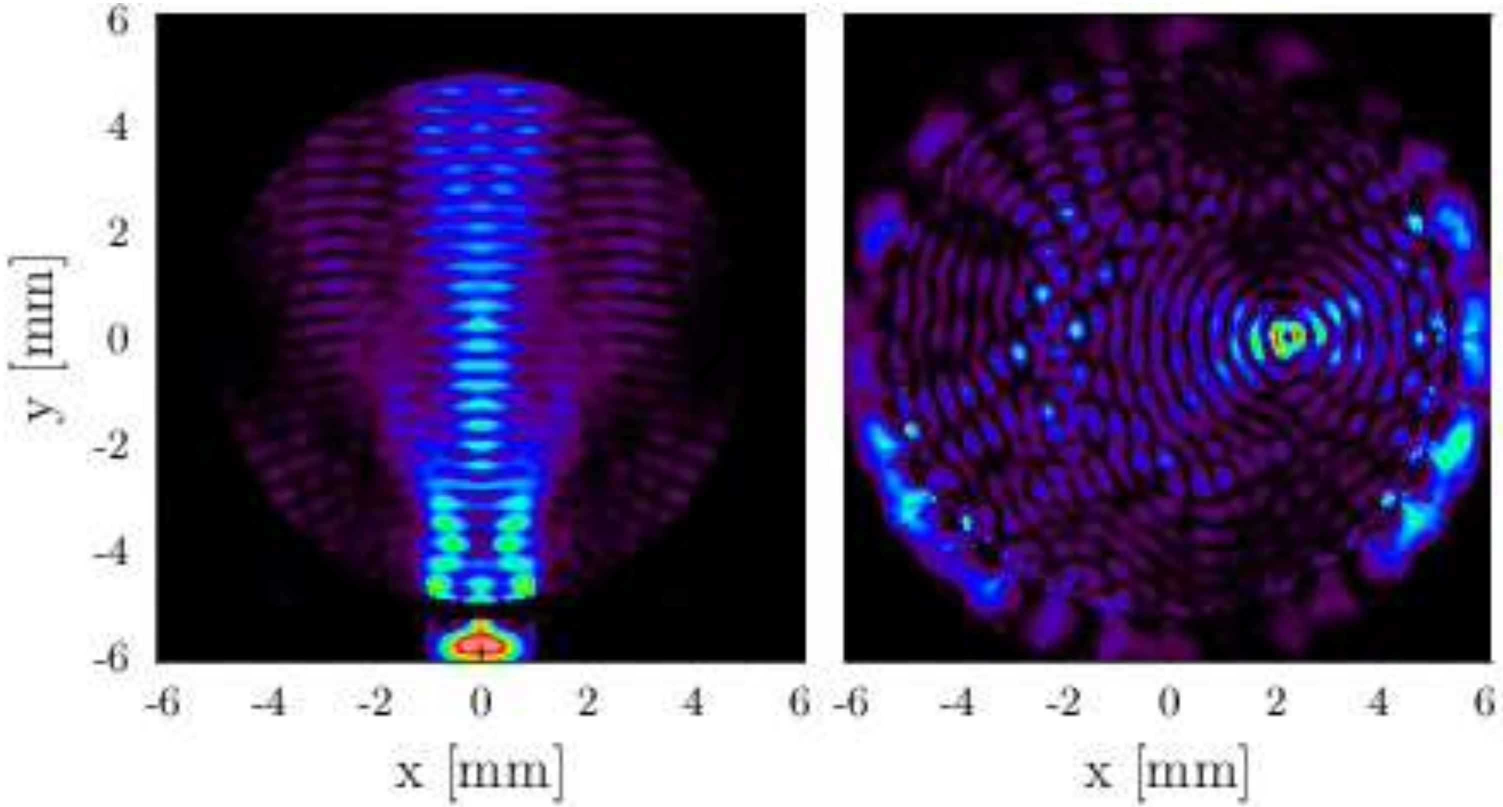
$$V_{nm} = V_0 \exp\left(i(\omega t + \phi_{nm})\right)$$

- Linear superposition.

$$V_n = \sum_{m=1}^{M} V_{nm} = V_n^{'} \exp\left(i\phi_n^{'}\right)$$



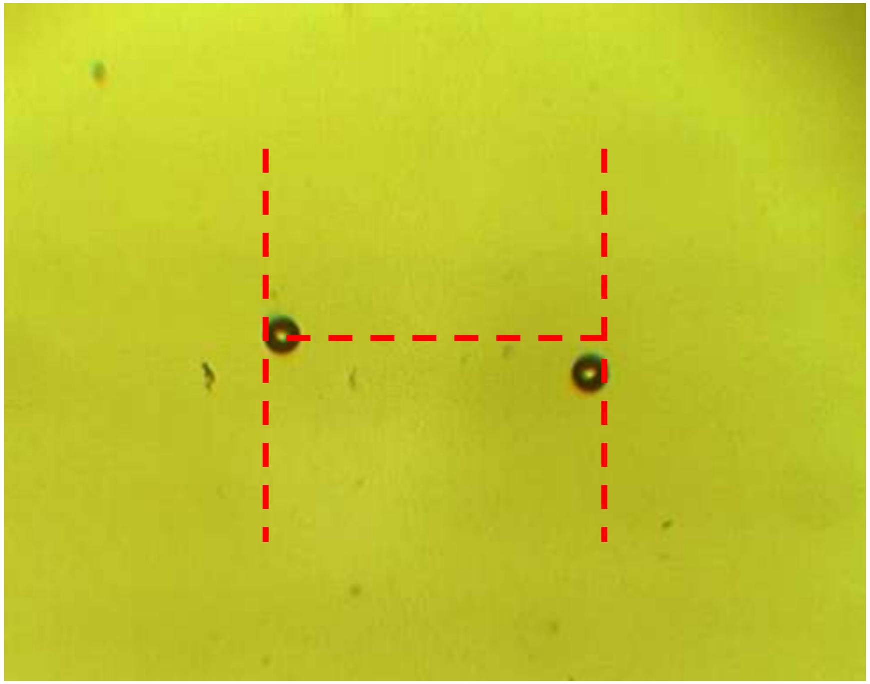
Full FE simulation of 32-element array device



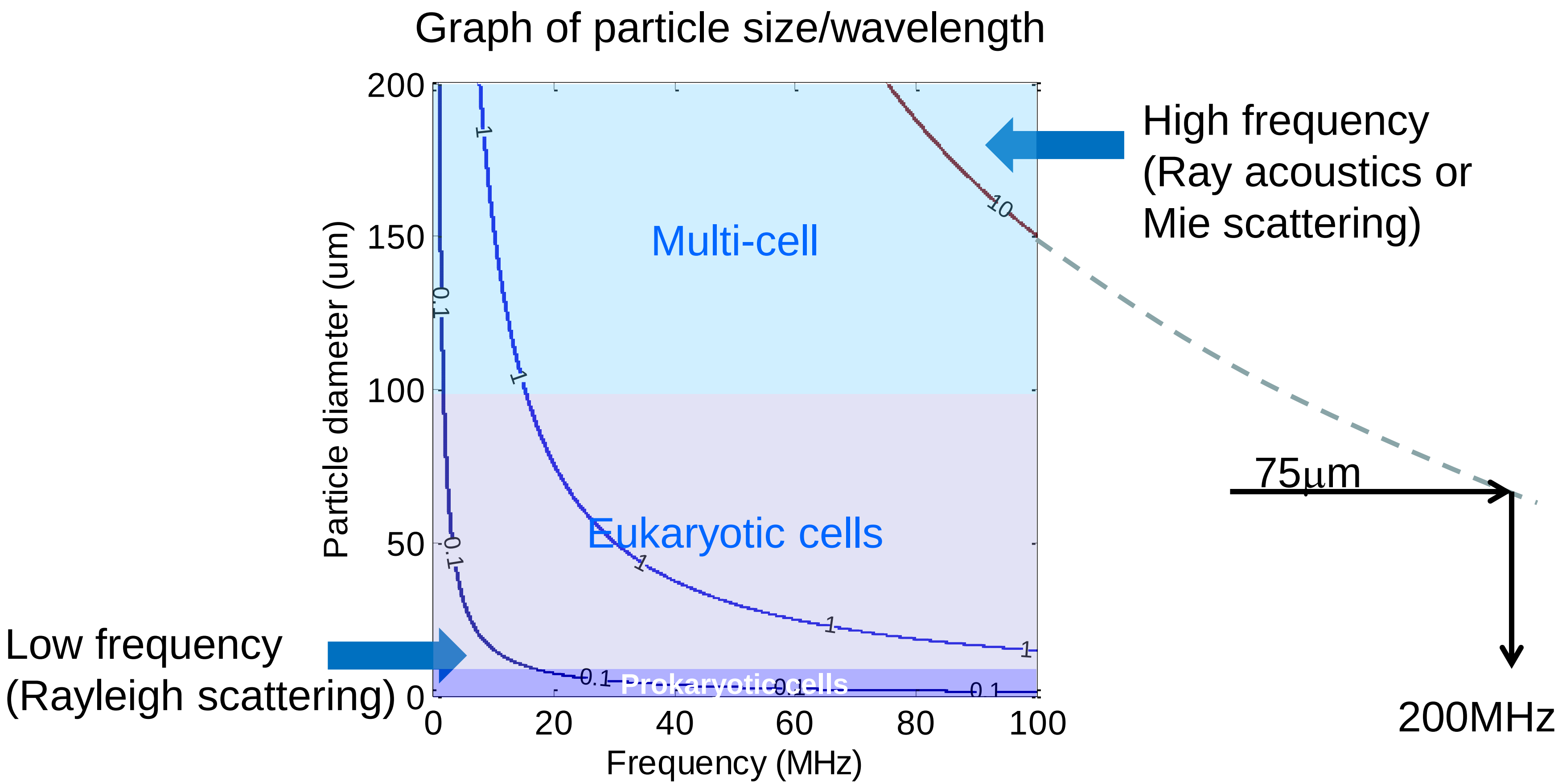
2 traps moving and merging

Schlieren

Video

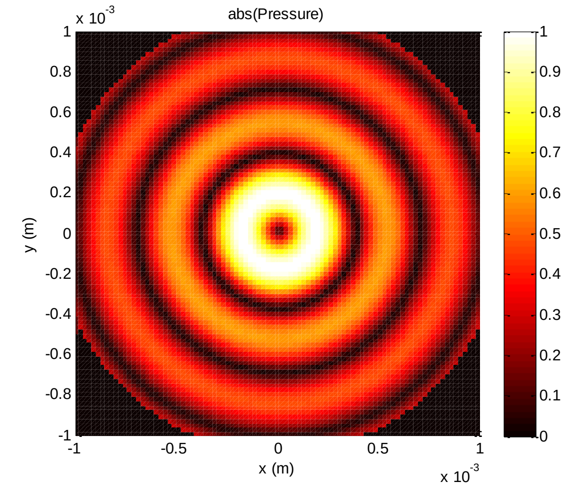


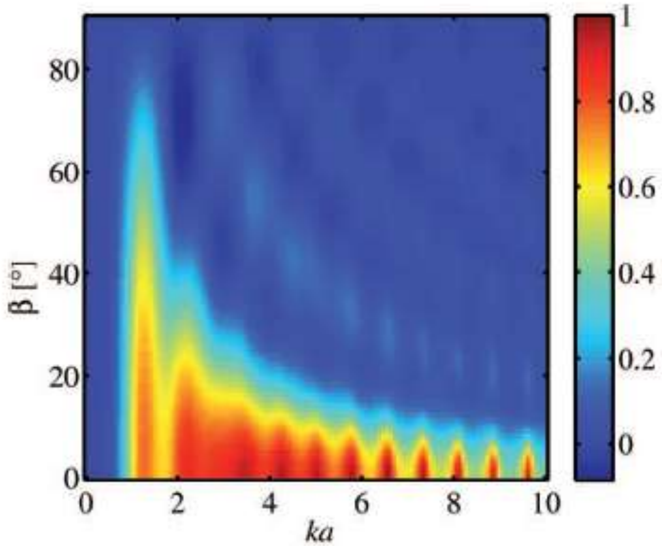
What does high and low frequency mean in practice?

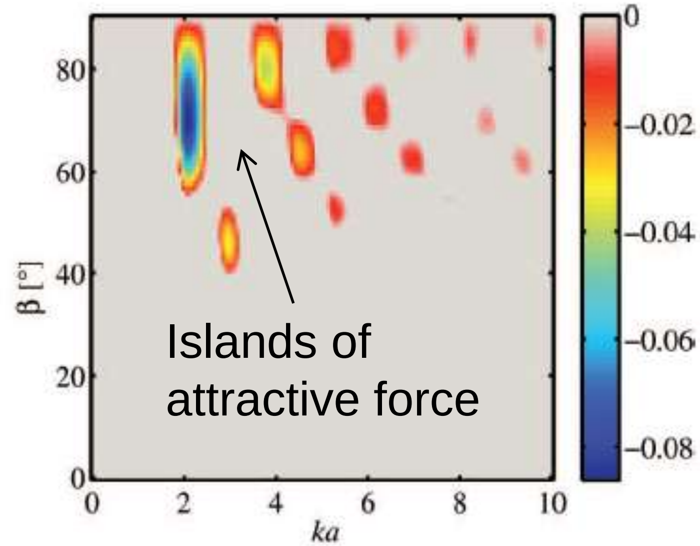


Propagating Bessel beams

$$p = e^{ikz\cos\beta} J_\alpha(k\rho\sin\beta) e^{i\alpha\varphi}$$

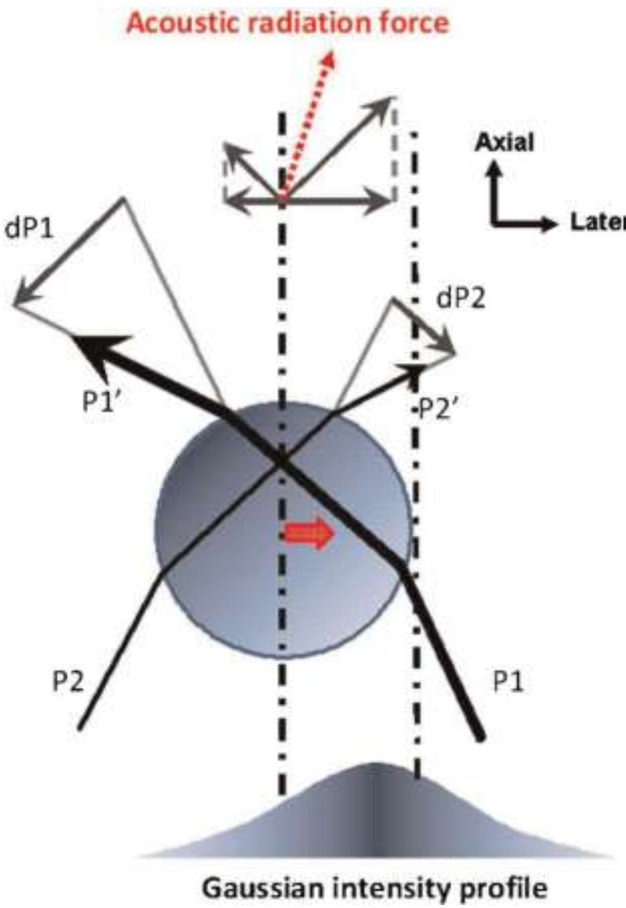






Silva et al in IEEE UFFC 60(6), 2013

High frequency force regime

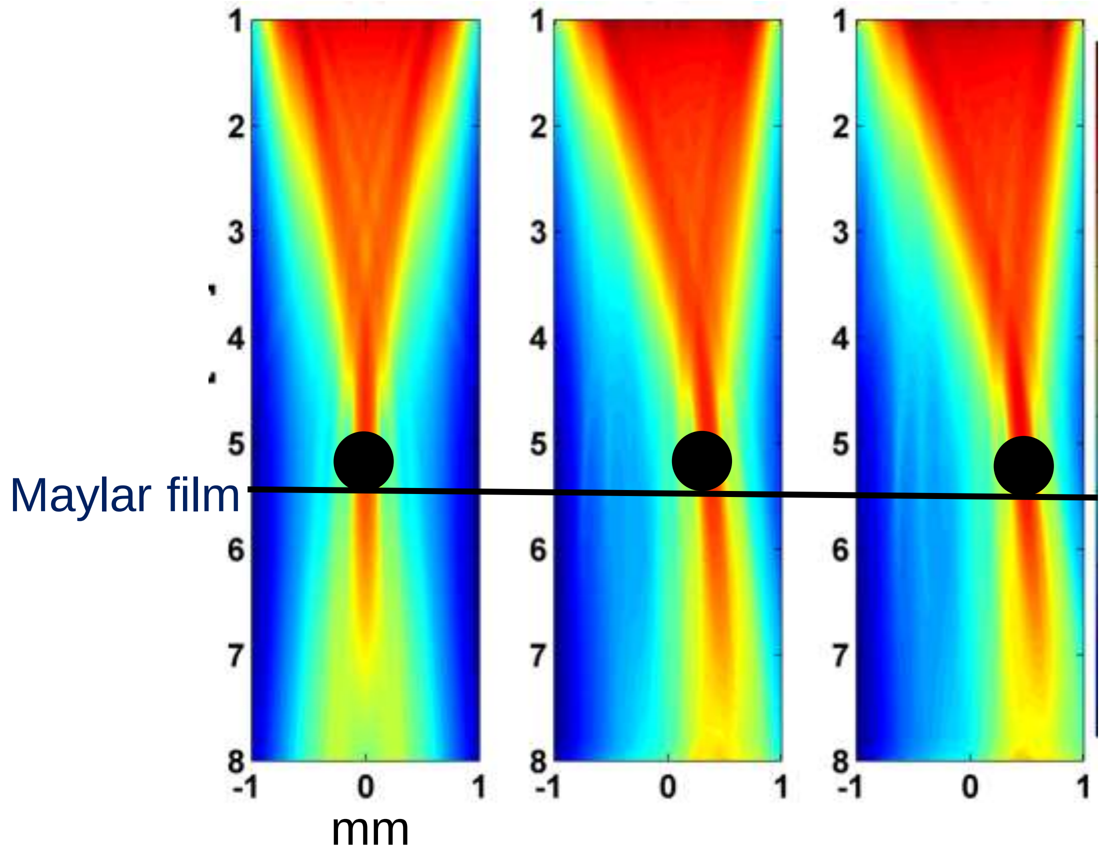


- $a \gg \lambda$ (ray acoustics)
- In 2010 Lee et al trapped a125μm lipid drop using 30MHz ultrasound (λ=60μm)
- In 2011 Lee et al[+] trapped a Leukaemia cell (10μm) using 200MHz ultrasound (λ=7.5μm)

*Lee et al (USC), IEEE UFFC, 57(10), 2010
+Lee et al (USC), Biotechnology and Bioengineering, 108(7), 2011

High frequency array

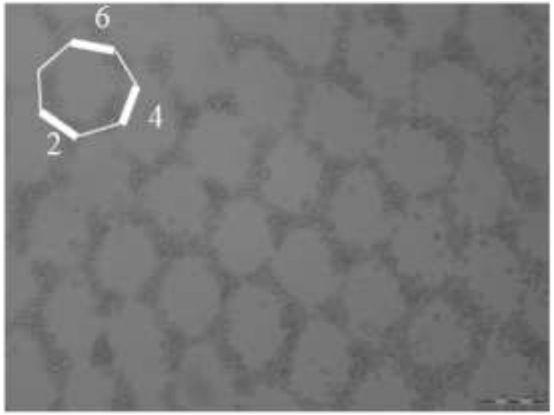
- 26MHz (λ=58μm), 64 element array*
- Ø 45μm PS
- Standard phased array focussing



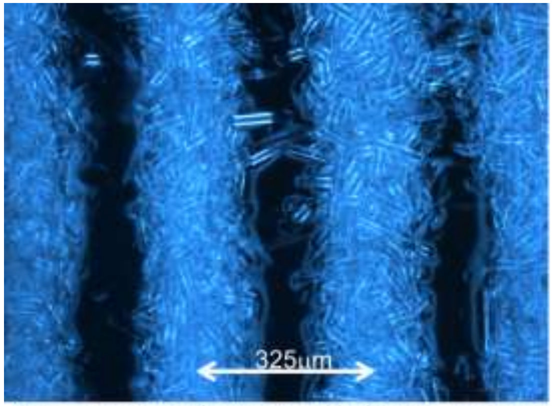
*Zheng et al (USC), APL 101, 2012

Applications

- Biology (e.g. tissue engineering)
  - High precision, high dexterity
  - Scale fixed by cell/tissue size
  - Non-destructive to cells
- Medicine (e.g. drug delivery)
  - Moderate precision, moderate dexterity
  - Scale fixed by delivery agent
  - Single sided
  - Destructive?
- Materials (e.g. composites)
  - Moderate precision, moderate dexterity
  - Large area, multi-scale
  - Fast
  - Flexible in terms of materials
  - No living matter involved

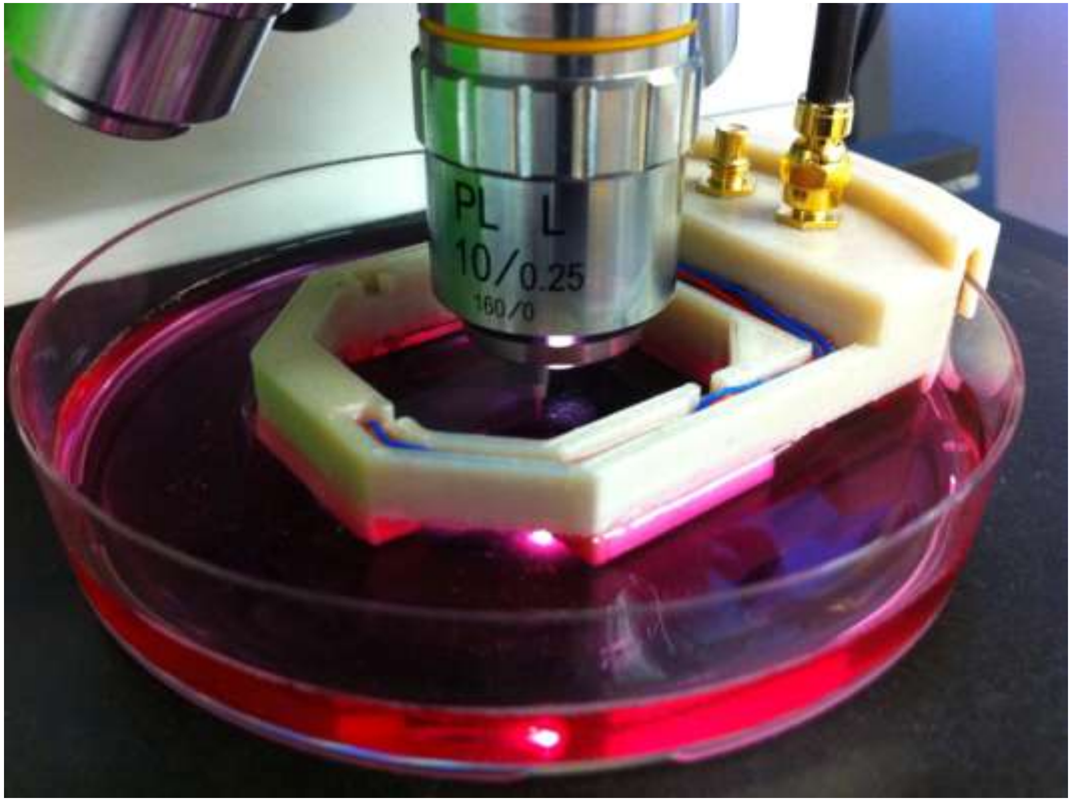


MDCK Cells (Photo courtesy of Anne Bernassau, University of Glasgow)



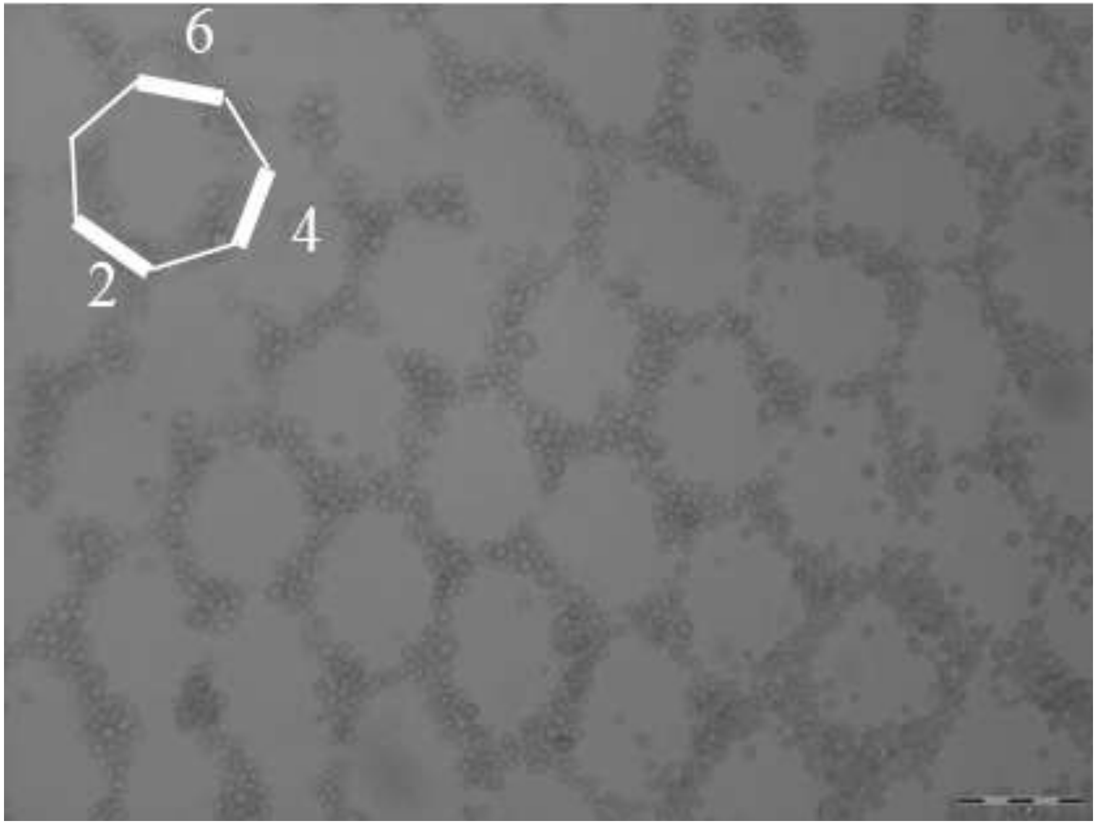
Glass fibres set in epoxy resin (Photo courtesy of Marc Scholz, University of Bristol)

Cell patterning



- Biocompatible acoustic manipulator printed with rapid prototyping system
- Fits within a petri dish
- 15x15mm active area
- Easy to sterilise
- Good optical access

Cell patterning

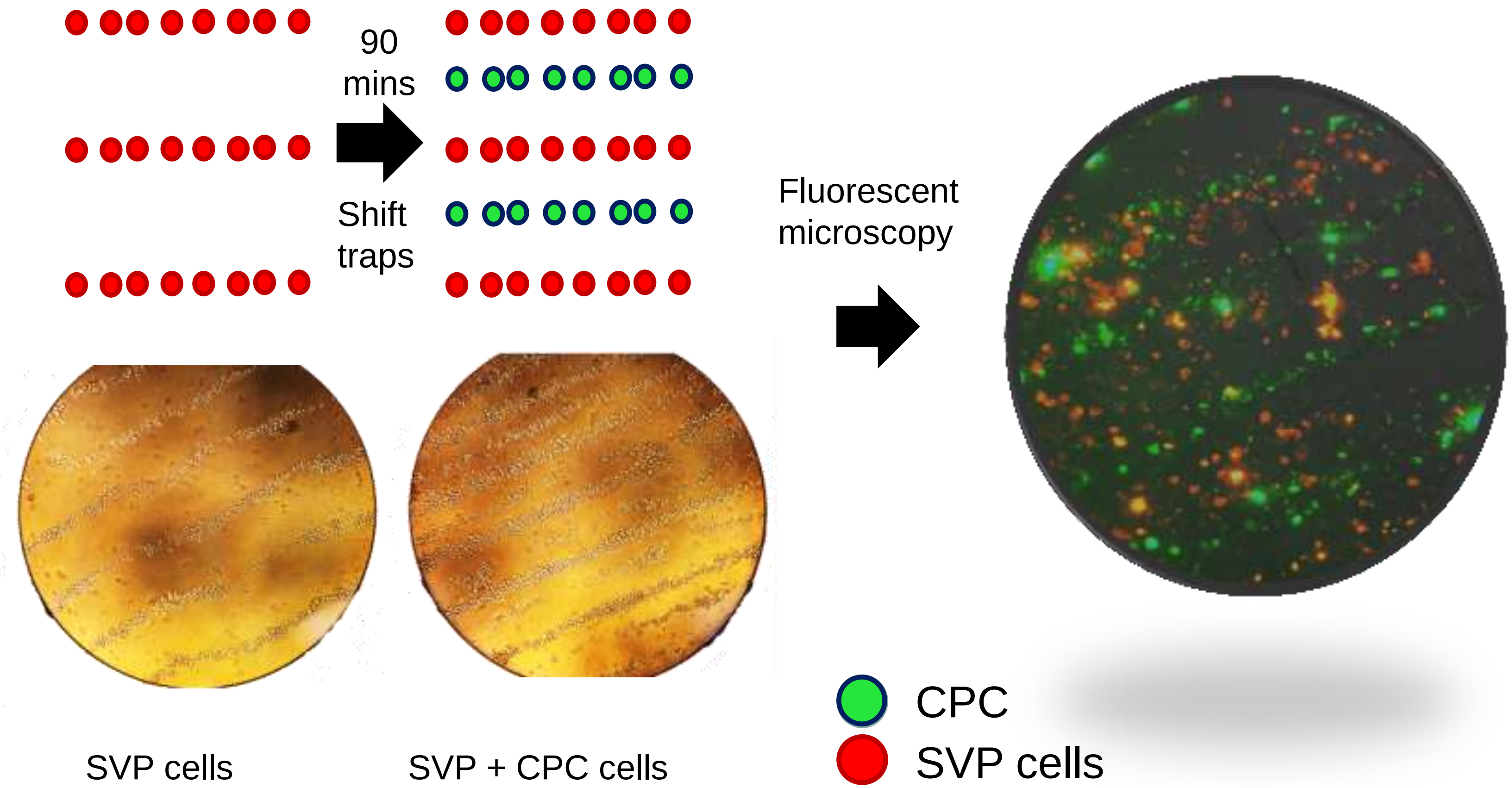


MDCK Cells (Photo courtesy of Anne Bernassau, University of Glasgow)

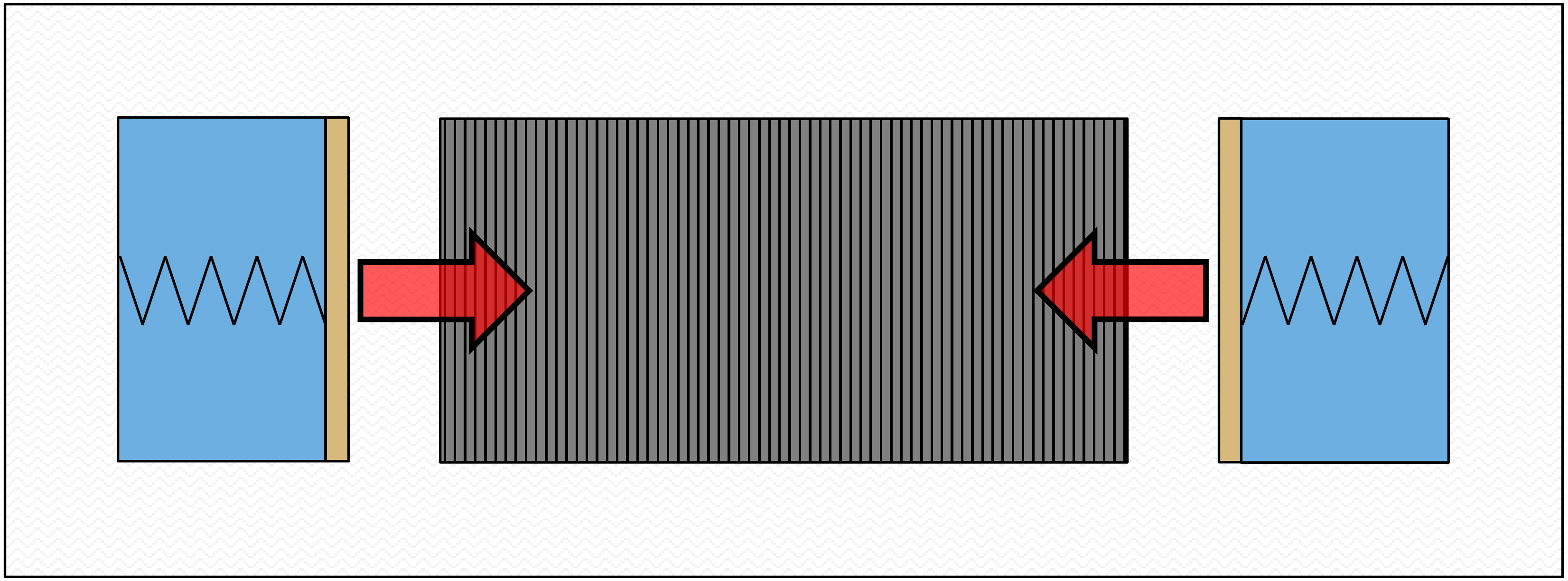
Uses include;

- Cell-cell and cell-chemical interaction studies
- Forming the building blocks of engineered tissue
- Various new migration and/or adherence assays

Co-culturing cells



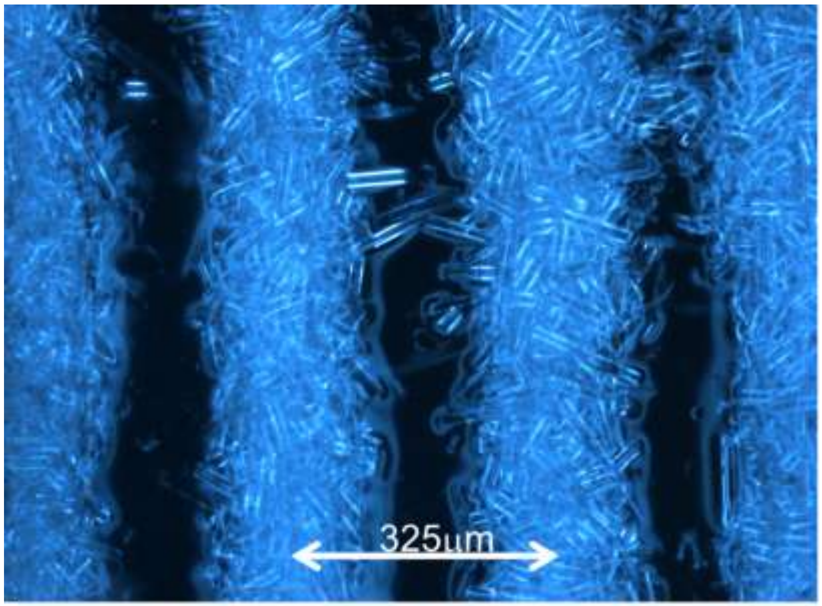
Composite manufacture



- Low viscosity photo-cure epoxy resin
- 15μm diameter, 50 μm length glass fibres
- Operated at 2MHz, so line spacing equals 325μm

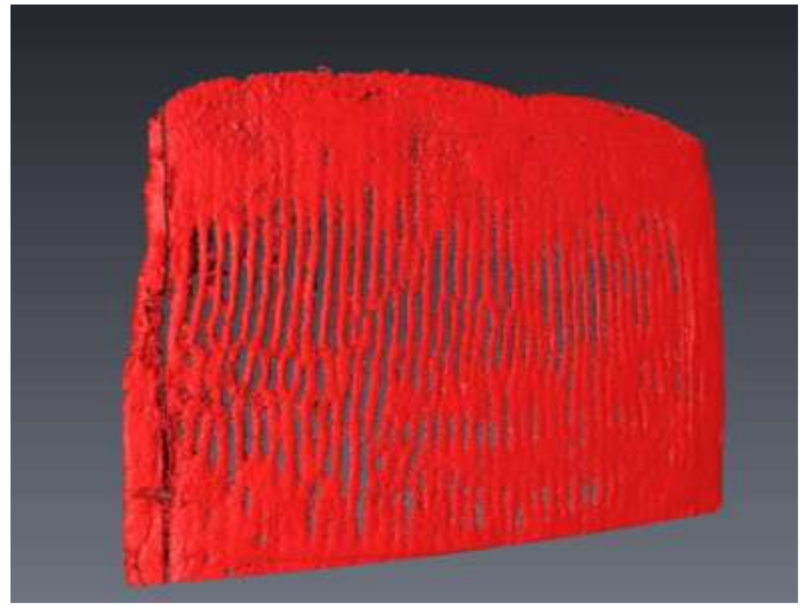
Composite manufacture

Photo



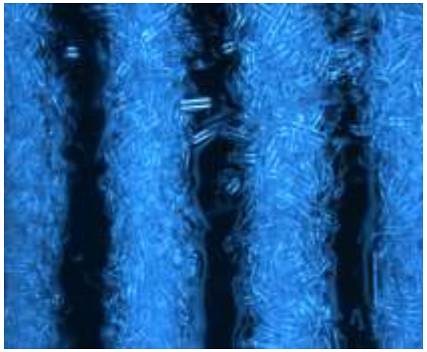
Glass fibres set in epoxy resin (Photo courtesy of Marc Scholz, University of Bristol)

X-ray CT



Concluding remarks

- Dexterous acoustic tweezing is a reality
- Various concepts are being explored and showing significant promise
- Typically devices use wavelengths ~100μm to manipulate cells ~10 μm in water (i.e. complimentary to optical tweezers)
- Order of magnitude variation in these length scales is possible
- Applications includes tissue engineering and micro/nano fabrication



IEEE Ultrasonics, Ferroelectrics, and Frequency Control Society

How to make an acoustic tweezer

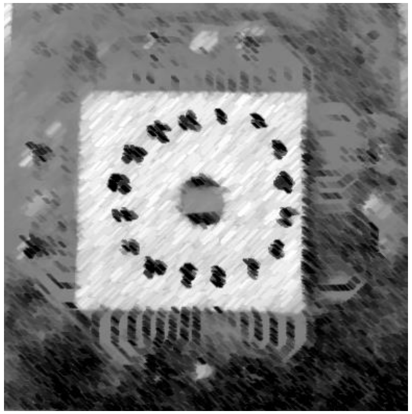
Professor Sandy Cochran
University of Dundee, UK

IEEE International Ultrasonics Symposium
Prague, Czech Republic
21 July 2013

Course Outline

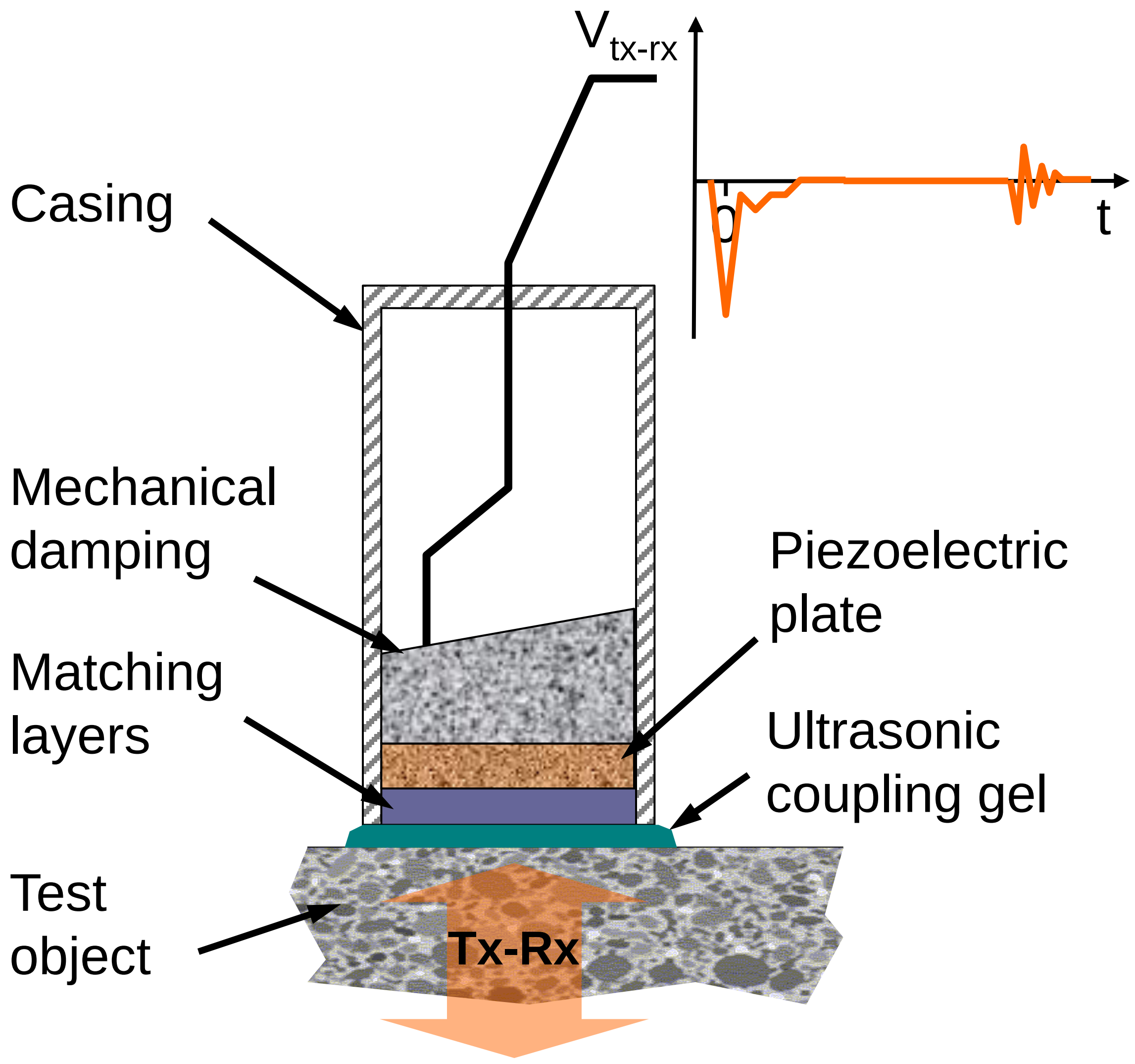
- This part of the course focuses on Sonotweezers as **arrays of individual devices**
  - Acoustic tweezing and sonotweezing may also refer to simpler devices
- The components of a **Sonotweezer**
  - The tweezer itself
    - Piezoelectric material
      - Micromachining
    - Other components
  - The **electronics**
    - Conventional multichannel excitation
    - Array controllers
    - Maximally simplified electronics
  - **Ancillary components**

The Components of a Sonotweezer



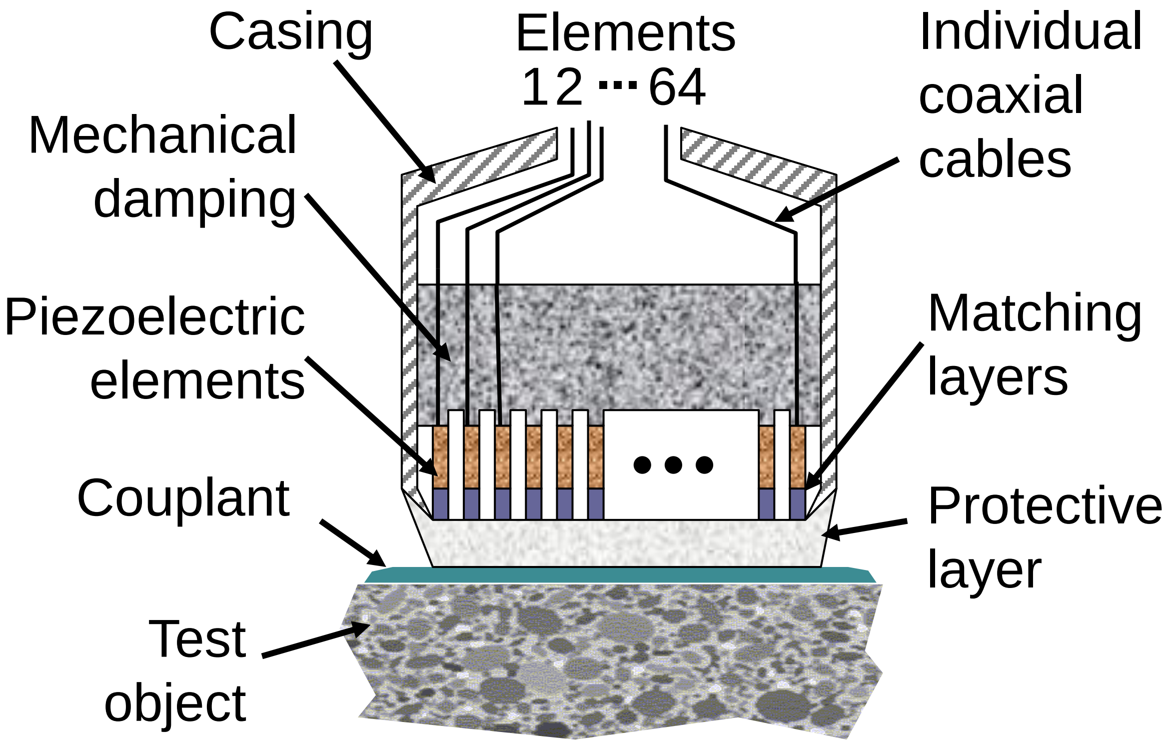
Conventional Transducer Structure

- Classic **single element** transducer



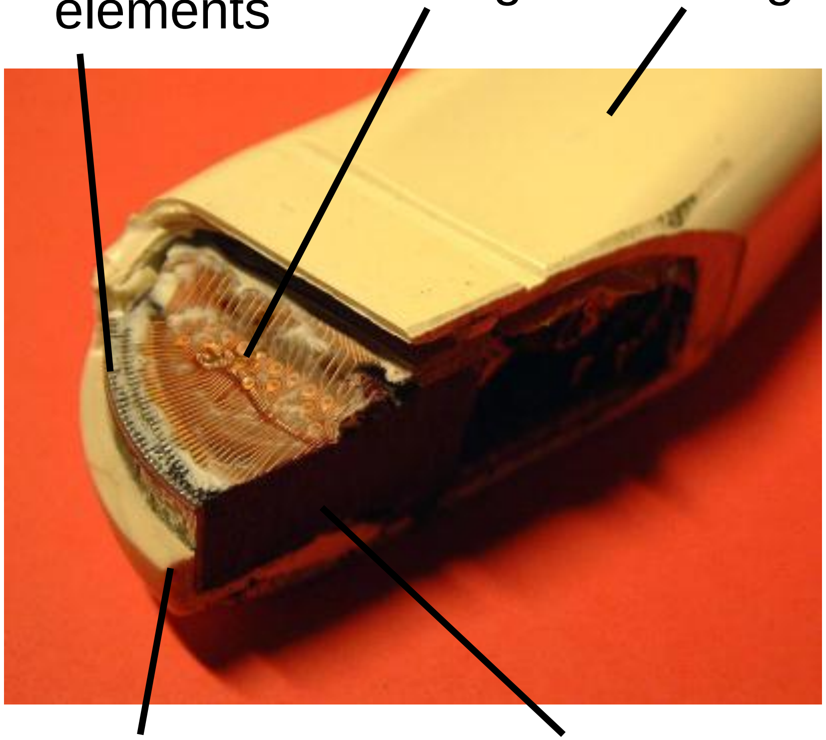
Ultrasonic Array Structure

- An array is a **set of miniature transducers** known as array elements
- The array elements are in **fixed, known positions** relative to one another



Medical Implementation

- Arrays are implemented with an **integrated manufacturing process**
  - The array is first made with all the elements joined together, using monolithic pieces of the active material and other layers
    - The elements are **separated in situ**
  - This approach is also ultimately the **only practical one** for Sonotweezers

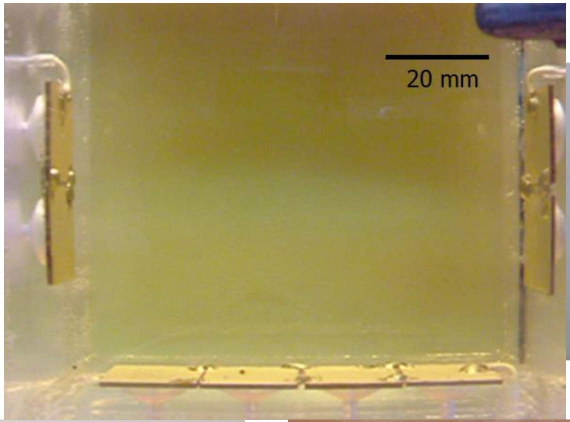


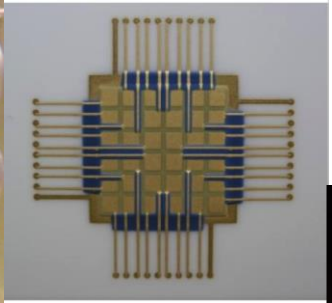
Sonotweezer Arrays

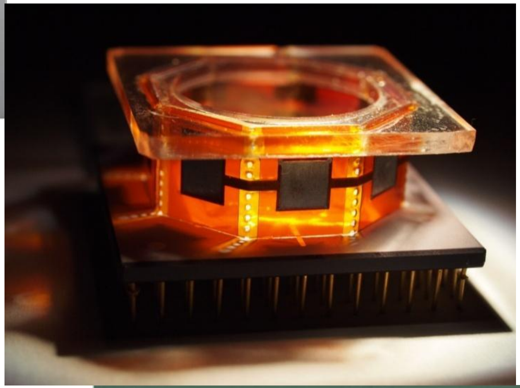
- **Piezoelectric elements**
  - Still required as a set of miniature transducers
    - Individual electrical connections also a necessity
- **Mechanical damping**
  - Acoustic tweezers are narrowband ultrasound sources
    - Hence mechanical damping is not needed
- **Matching layers**
  - Needed for some acoustic tweezers but not all
    - Can be omitted for simple, exploratory devices
- **Casing etc**
  - Designed ad hoc according to application
  - Unlikely to require protective front face layer

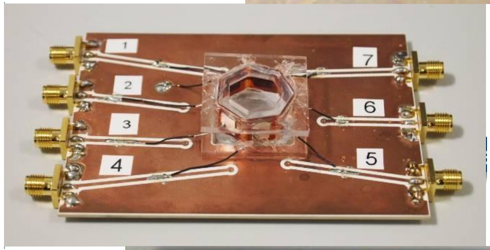
Examples

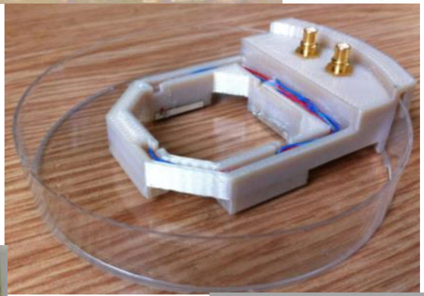
Not to scale

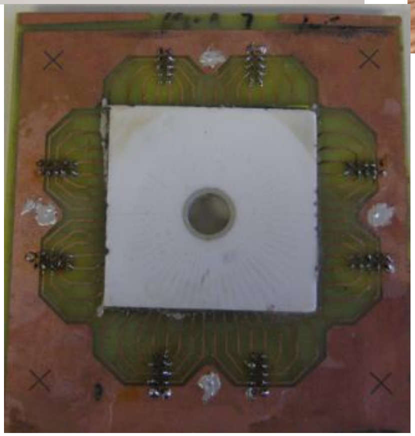


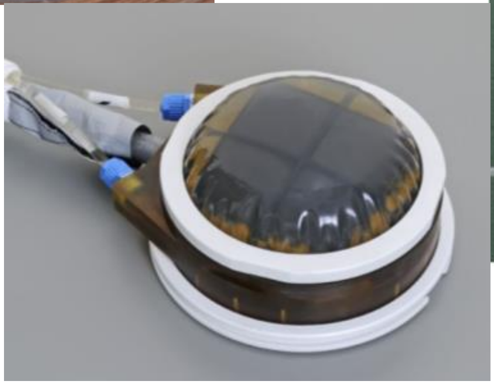


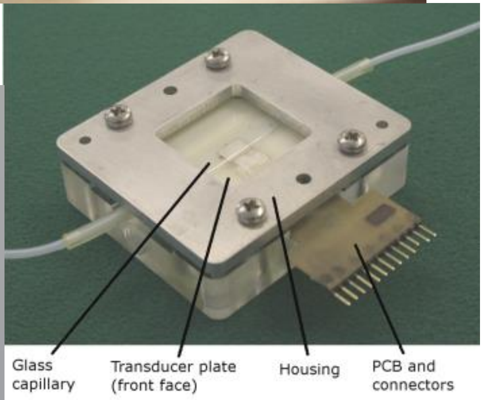








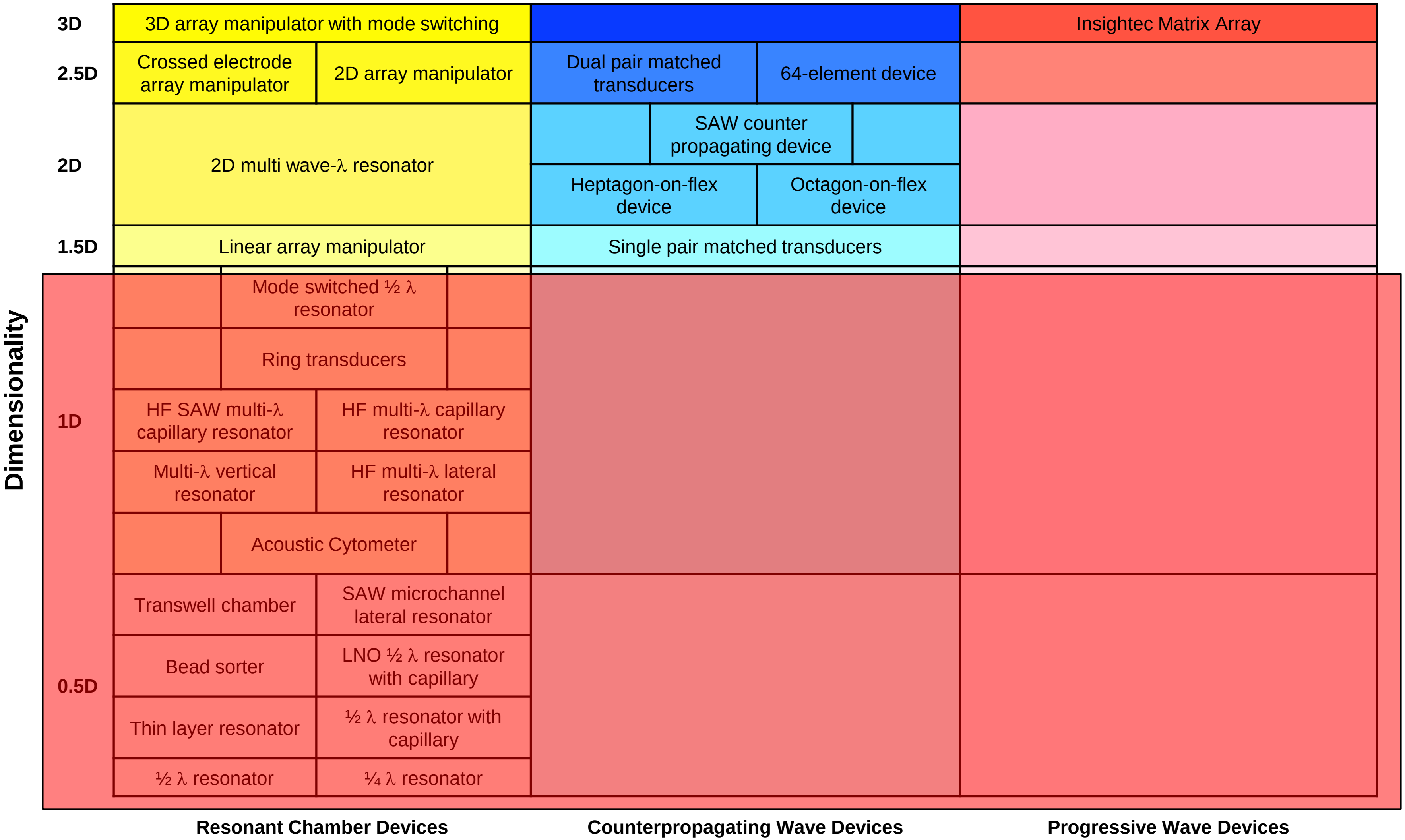




Related Design Framework

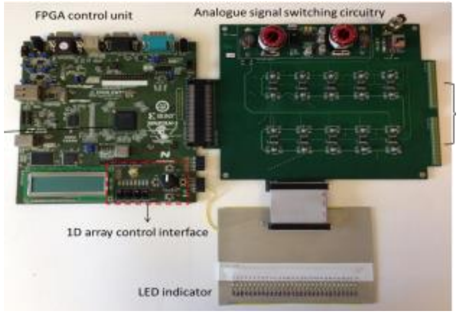
Dimensionality	Resonant Chamber Devices	Counterpropagating Wave Devices	Progressive Wave Devices
3D	3D array manipulator with mode switching		Insightec Matrix Array
2.5D	Crossed electrode array manipulator 2D array manipulator	Dual pair matched transducers 64-element device	
2D	2D multi wave-λ resonator	SAW counter propagating device Heptagon-on-flex device Octagon-on-flex device	
1.5D	Linear array manipulator	Single pair matched transducers	
1D	Mode switched ½ λ resonator Ring transducers HF SAW multi-λ capillary resonator HF multi-λ capillary resonator Multi-λ vertical resonator HF multi-λ lateral resonator Acoustic Cytometer		
0.5D	Transwell chamber SAW microchannel lateral resonator Bead sorter LNO ½ λ resonator with capillary Thin layer resonator ½ λ resonator with capillary ½ λ resonator ¼ λ resonator		

Related Design Framework



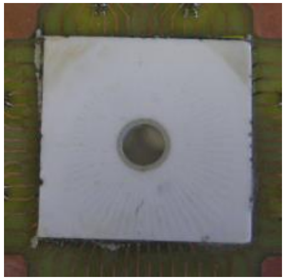
Electronics

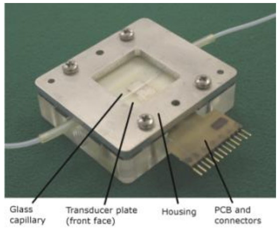
- Three choices
  1. Based on commercial **multichannel signal generators**
     - May need additional output amplification
  2. A commercial ultrasound **array controller**
     - Typically supplied for nondestructive testing
       - May not have sufficient drive capability
     - Alternative is system for focused ultrasound surgery
       - Likely to be low frequency / high power
  3. Fully **custom electronics**
     - Field programmable gate array (FPGA) control likely to be essential
       - With additional simple analogue electronics

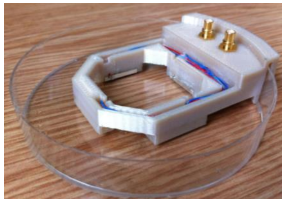


Ancillary Components

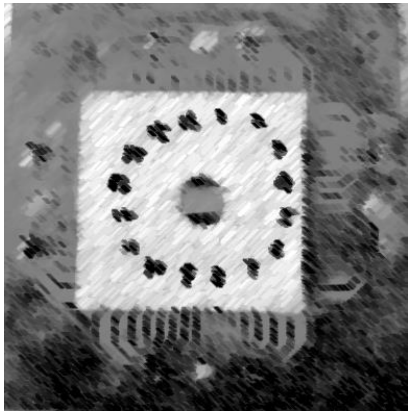
- Some Sonotweezers may contain the working fluid and cells within their structure
  - These devices will either have to be experimental or disposable
- As an alternative, detachable components can be used to contain the working fluid
  - A very wide range of **glass capillaries** is readily available
    - These are inexpensive, mass produced items suitable as **disposables**
    - Their **dimensions can vary significantly** relative to acoustic requirements
  - A Sonotweezer can be designed to fit in a **petri dish**
  - Other specific plastic or glass components could be manufactured







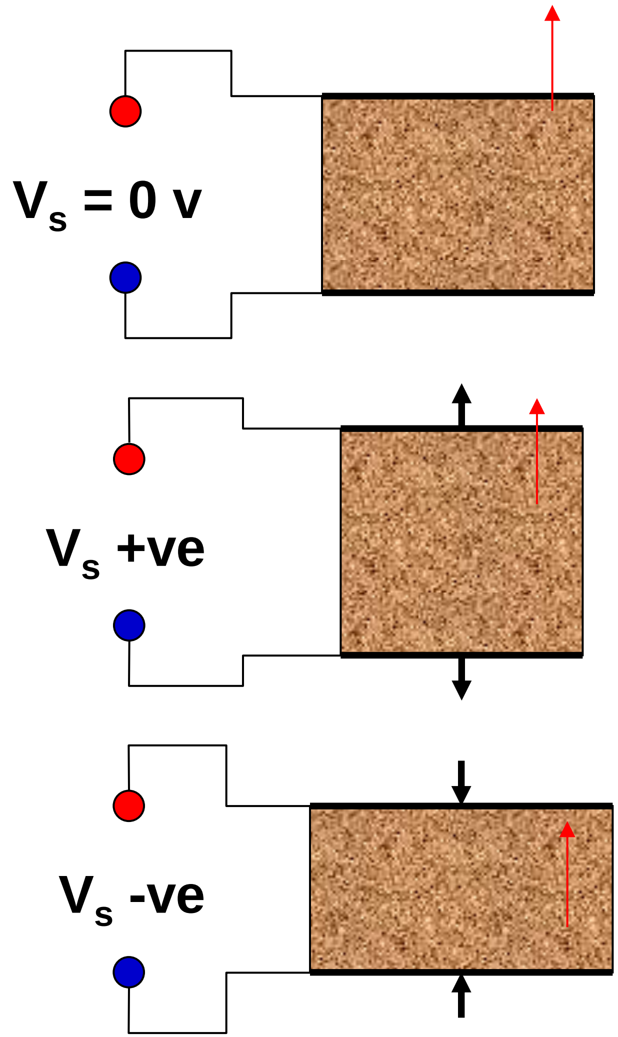
The Tweezer Itself



Piezoelectric Material

- Tweezers need **pressure to be generated** in response to an applied voltage
- **Converse** piezoelectric effect:

  When a voltage is applied to a piezoelectric material external pressure is generated
- The relevant parameter is d, the **piezoelectric charge coefficient** (units NC^{-1} or mV^{-1})
  - Typical value $d_{33} = 600\ pmV^{-1}$



Possible Piezomaterials

			PZT-4	PZT-5H	PVDF	$LiNbO_3$	PMN-PT
			"Hard" piezoelectric ceramic	"Soft" piezoelectric ceramic	Piezoelectric polymer	Traditional single crystal	New, high performance single crystal
Stiffness	c_{33}^D	GNm^{-2}	155	159	8.52	251	135
Density	ρ	kgm^{-3}	7500	7500	1760	4640	8000
Velocity	v	ms^{-1}	4560	4600	2200	7360	4040
Acoustic impedance	$Z = \rho v$	MRayl	34.1	34.5	3.92	34.1	32.3
Piezoelectric strain constant	d_{33}	pmV^{-1}	289	593	25	5.88	1430
Piezoelectric voltage constant	g_{33}	VmN^{-1}	26	20	230	22	30
Piezoelectric figure of merit	FOM = $d_{33}.g_{33}$	pmN^{-1}	7.51	11.9	5.75	0.129	42.8
Thickness mode coupling coefficient	k_t		0.508	0.512	0.190	0.162	0.566
Length-extensional coupling coefficient	k_{33}		0.691	0.746	0.130	0.162	0.897
Relative permittivity at constant stress	ε_{33}^T		1275	3430	8.4	29.8	3950
Relative permittivity at constant strain	ε_{33}^S		638	1470	10-12	29.0	818
Mechanical quality factor	Q		High	Medium	Low	Very high	Low

All values are *indicative only*

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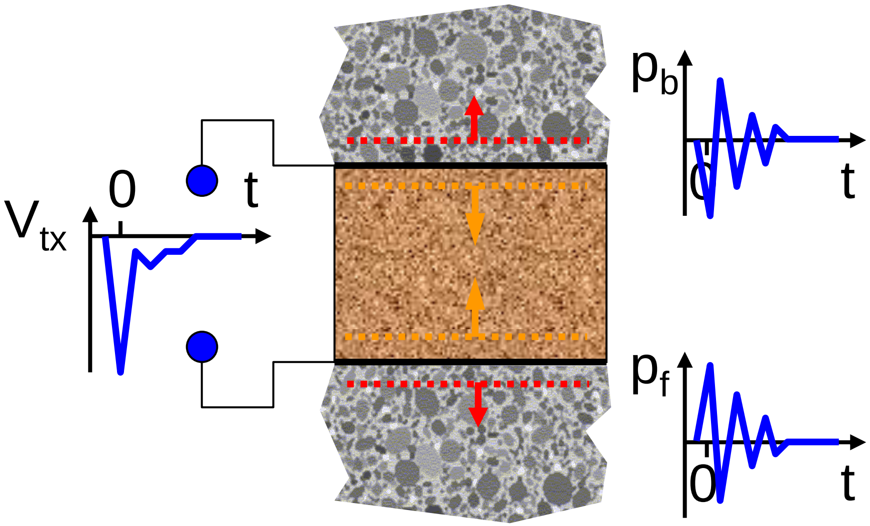
All values are *indicative only*

Internal and External Waves

- Excitation voltage, V_{HV}, is applied, with **desired spectral content**, e.g. sine wave for burst output
- Four distinct mechanical waves are set up
  - Two propagating in the **external media**
  - Two propagating within the **piezoelectric material**



- The waves in the piezoelectric material are **partially internally reflected**, creating an oscillating condition and resonance, with a **frequency inversely proportional to thickness**

Mechanical Resonance

- **Mechanical resonance** is a fairly straightforward physical effect
  - Hence the frequency, f_m, is easily determined

$$\lambda = 2D$$

$$f_m = \frac{v}{\lambda}$$

where

λ = acoustic wavelength

D = thickness of piezoelectric material

v = acoustic velocity in piezoelectric material

- This **ignores** issues such as piezoelectric stiffening and modification of wave propagation by component shape

Electrical Resonance

- As the piezoelectric material forms an electrical component (as well as mechanical i.e. it is electromechanical) it also has an **electrical resonance**
  - There is no particularly straightforward way to calculate f_e, the electrical resonance frequency
  - One way, for wide, thin plates, is to back f_e out of the expression for **thickness mode coupling coefficient**

$$k_t = \sqrt{\frac{\frac{\pi f_e}{2 f_m}}{\tan\left(\frac{\pi f_e}{2 f_m}\right)}}$$

- Because the elements in Sonotweezers are **small**, they are likely to **operate best at f_e**

Matching Layers

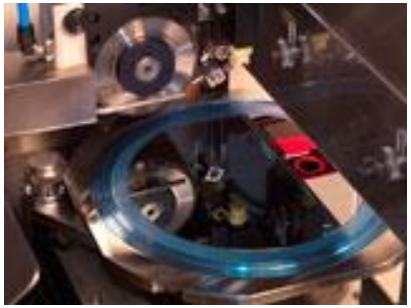
- Matching layers are designed to have **anti-reflective** properties to enhance energy transfer from the piezoelectric material through the
  couplant into the ultrasonic medium
- **Theoretically**, the thickness of a single matching layer, T_{ml} and its acoustic impedance, Z_{ml}, are defined as

$$T_{ml} = \lambda_{ml} / 4, \; Z_{ml} = \sqrt{(Z_{pm} Z_{um})}$$

  where λ_{ml} is the wavelength in the matching layer, and Z_{pm} and Z_{um} are the acoustic impedances of the piezoelectric material and the ultrasonic medium respectively
- Although a matching layer works ideally at only a single frequency, corresponding to λ_{ml}, it often **increases the operating bandwidth** by reducing reverberation in the piezoelectric material

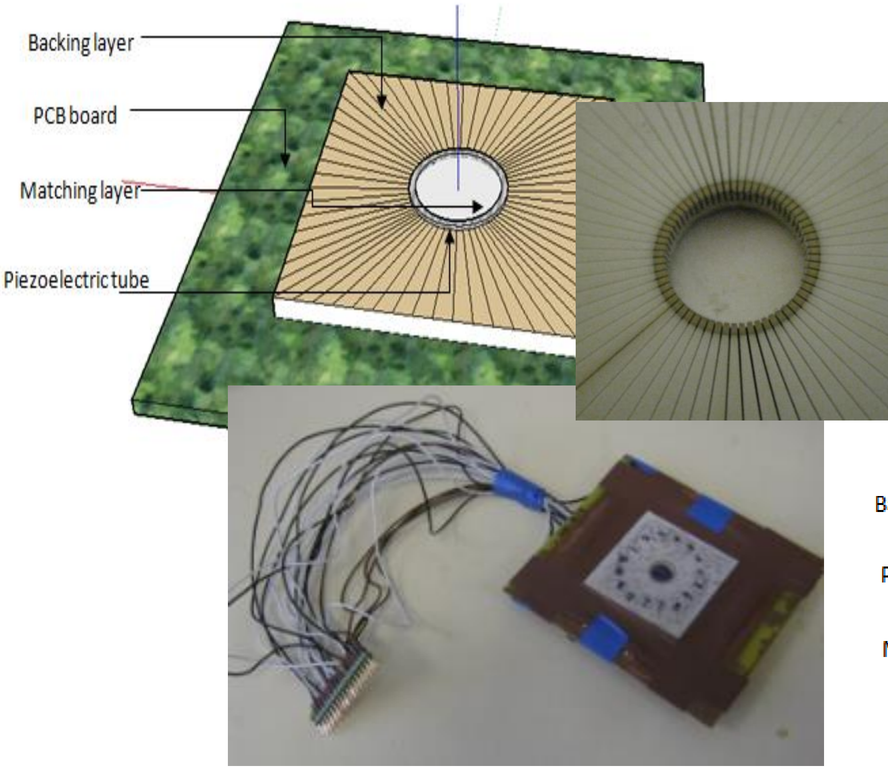
Micromachining

- Micromachining is needed to generate the **precise shapes** required for the piezoelectric material and the matching layer
- Three possible routes
  - Accessing a **conventional machine shop**
    - Problems with size of tools and machine precision
    - Problems with machining piezoelecric materials
  - Assembling or accessing a **specialised workshop**
    - Key components are dicing saw and lapping / grinding machines
    - Polymer handling / machining also required
  - Utilising **semiconductor / MEMS industry fabrication** processes
    - Highly restricted availability

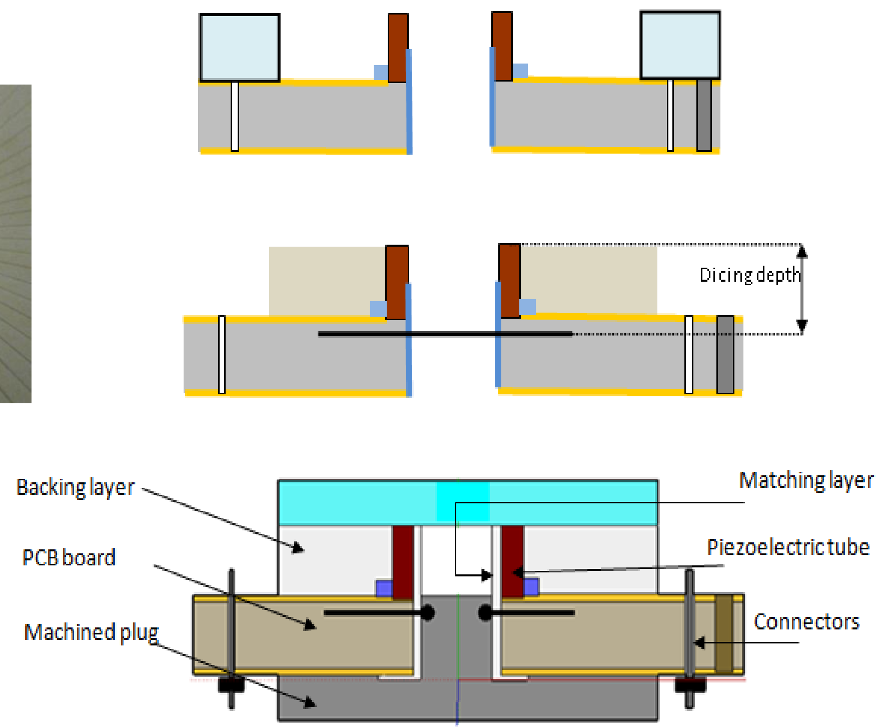


Example: 64-element Array

Basic design layout

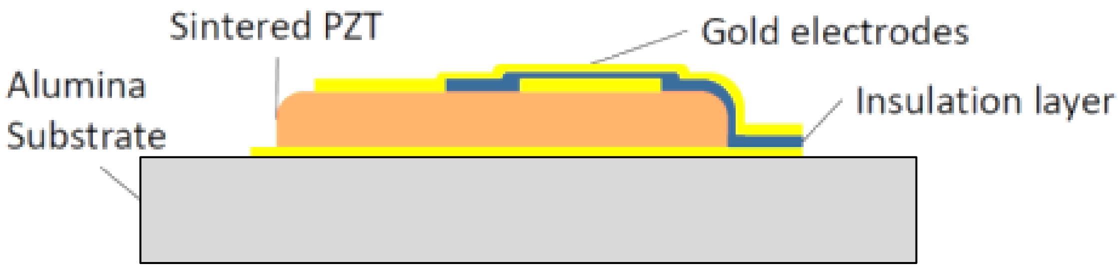


Fabrication process diagram



- Fabrication process is an **integrated** one
    - Matches **medical ultrasound** approach

Example: Thick Film Sonotweezer



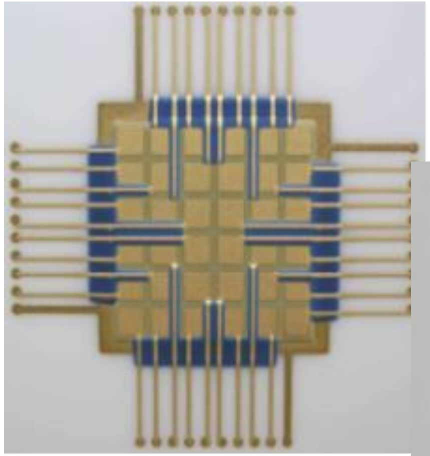
IKTS
Fraunhofer Institut Keramische Technologien und Systeme

Electrical interconnect

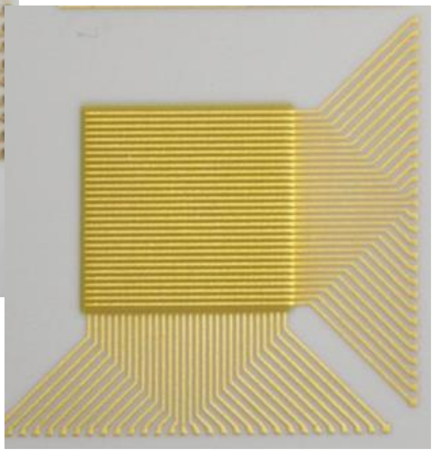
- PZT, Array electrodes and electrode tracks all screen printed on substrate
- Mask-based fabrication

Fluidic & optical interface

- Array forms base of chamber, or
- Capillary coupled to array

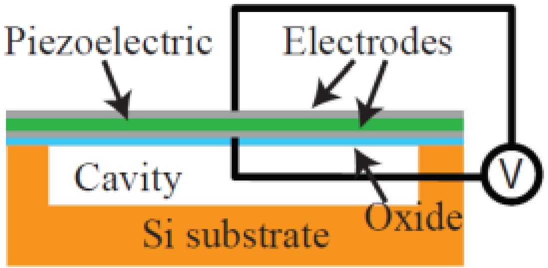


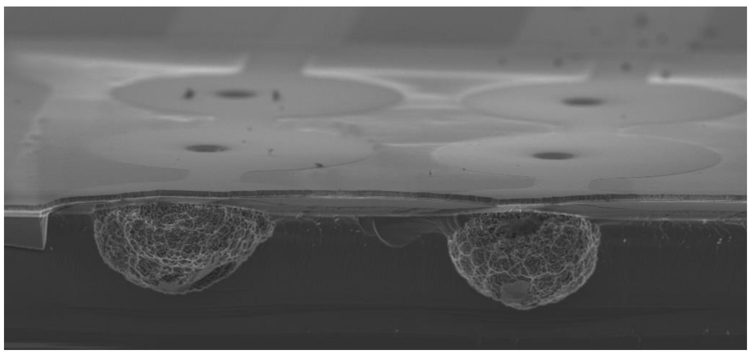
2D Array

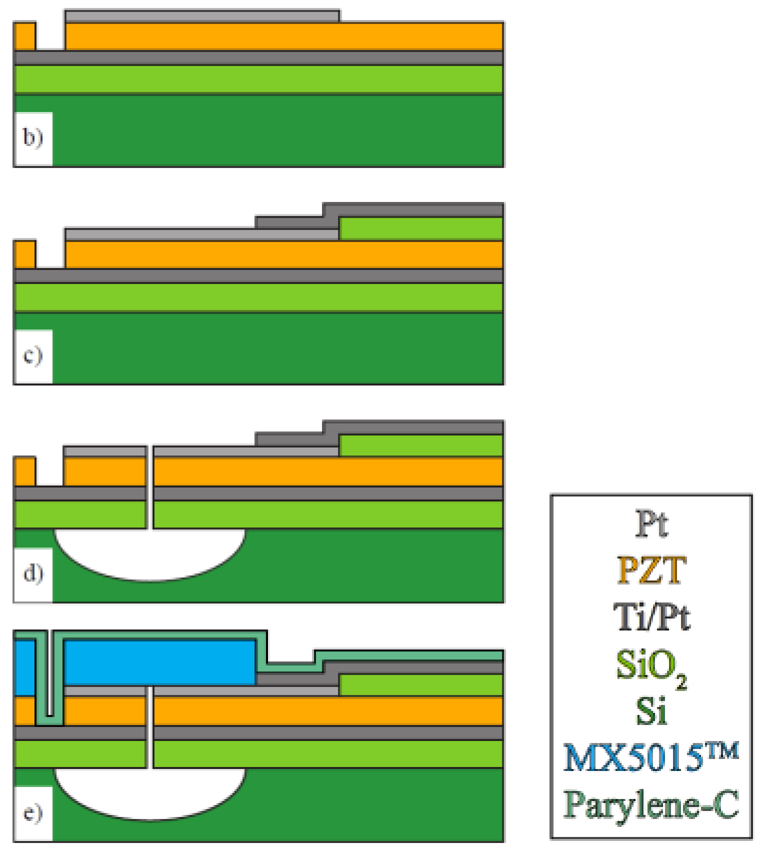


Crossed-electrode array

Example: pMUTs

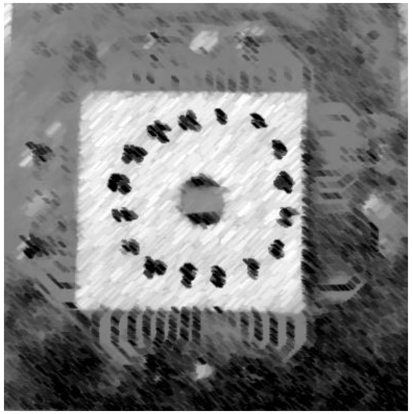






- Thin film deposition for PZT, array electrodes and electrode fan-out
- Fully mask-based fabrication
- Conventional Si-based microfabrication techniques can be used

Electronics for Sonotweezers



Commercial Signal Generators

- Advantages
  - Straightforward solution for **small numbers of elements**
  - Likely to provide **enough drive capability** without additional amplification
  - Offers **easy flexibility**
- Disadvantages
  - **Costly** because of need for flexibility in design
  - Feasible **maximum number of elements limited**
  - **Not** space efficient
  - **Multiple cables** needed: awkward and unreliable

Commercial Array Controller

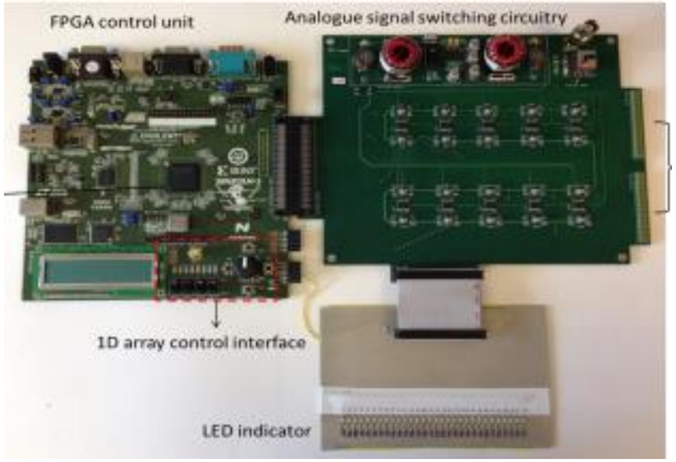
- Advantages
  - Should be able to support **enough channels**
  - Provides automatic channel **phasing / synchronisation**
- Disadvantages
  - **May be as costly as separate signal generators**
  - Typically not well matched to Sonotweezers application
    - Will usually include **unnecessary hardware** for reception
    - Will usually **not allow CW** excitation

www.diagnosticsonar.com

www.verasonics.com

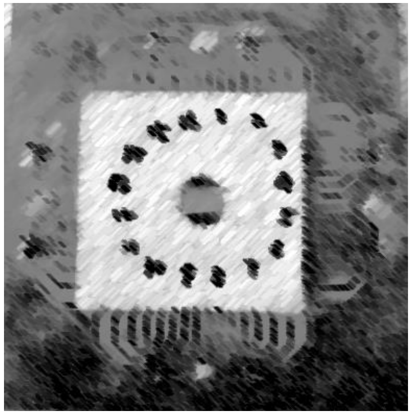
www.olympus-ims.com

Custom Electronics



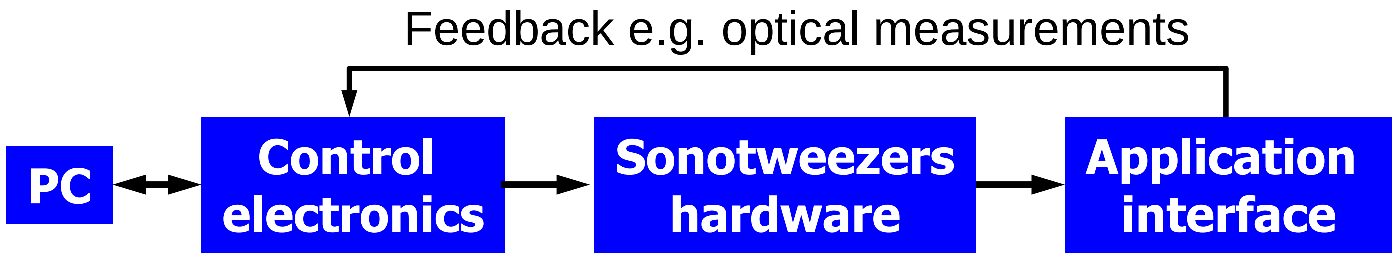
- Advantages
  - Relatively **inexpensive hardware**
    - **FPGA** evaluation board
    - Custom analogue drive board
      - Possible to drive Sonotweezers with **rectangular waveforms**
  - **Minimal hardware cost** per channel
  - Automatic **channel phasing** / synchronisation
- Disadvantages
  - **Low level programming** required - VHDL, or LabVIEW option
  - **Custom electronics design** and fabrication required
  - Large channel counts may need **complicated solutions**

Ancillary Components



Ancillary Components

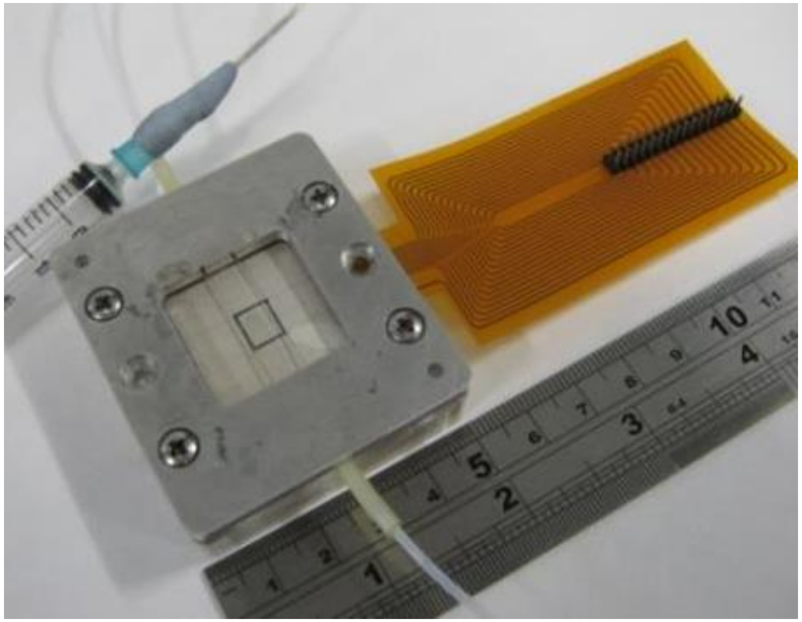
- Translation of Sonotweezers from electronics lab curiosity to useful system requires application-specific front end



- Must work with Sonotweezers
  - Likely also to have to provide additional access for **observation / measurement**
- Must provide access for **target of manipulation**
  - E.g. connection to syringe driver
- Likely to be **disposable** for work in life sciences
  - Capillary, cuvette or petri dish

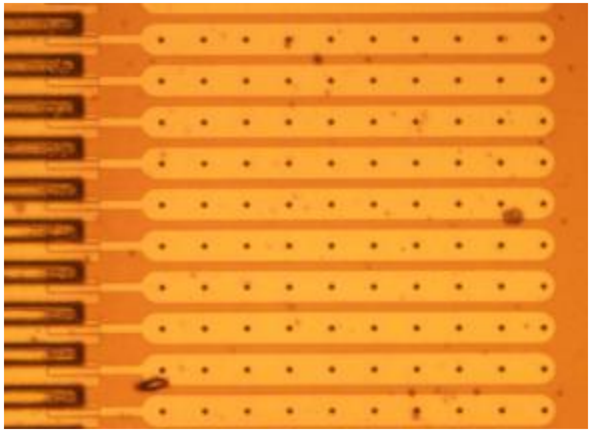
Example: 1D Array System

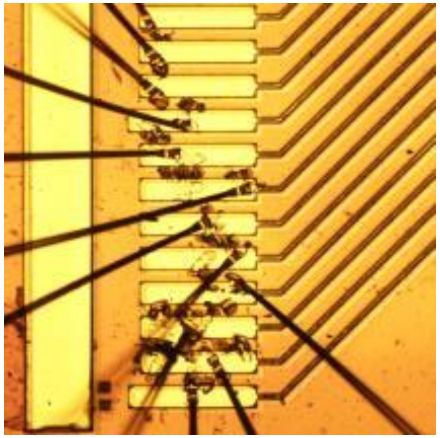
- Optical (**observation**) interface
    - Clear glass capillary with open window for microscope observation
- **Fluidic** interface
    - Capillary **coupled** to array substrate
    - Filled / flow controlled from **syringe**

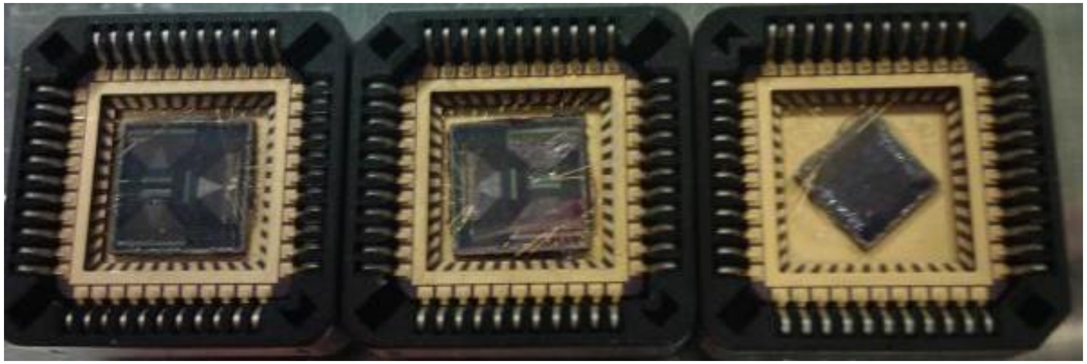


Example: pMUTs

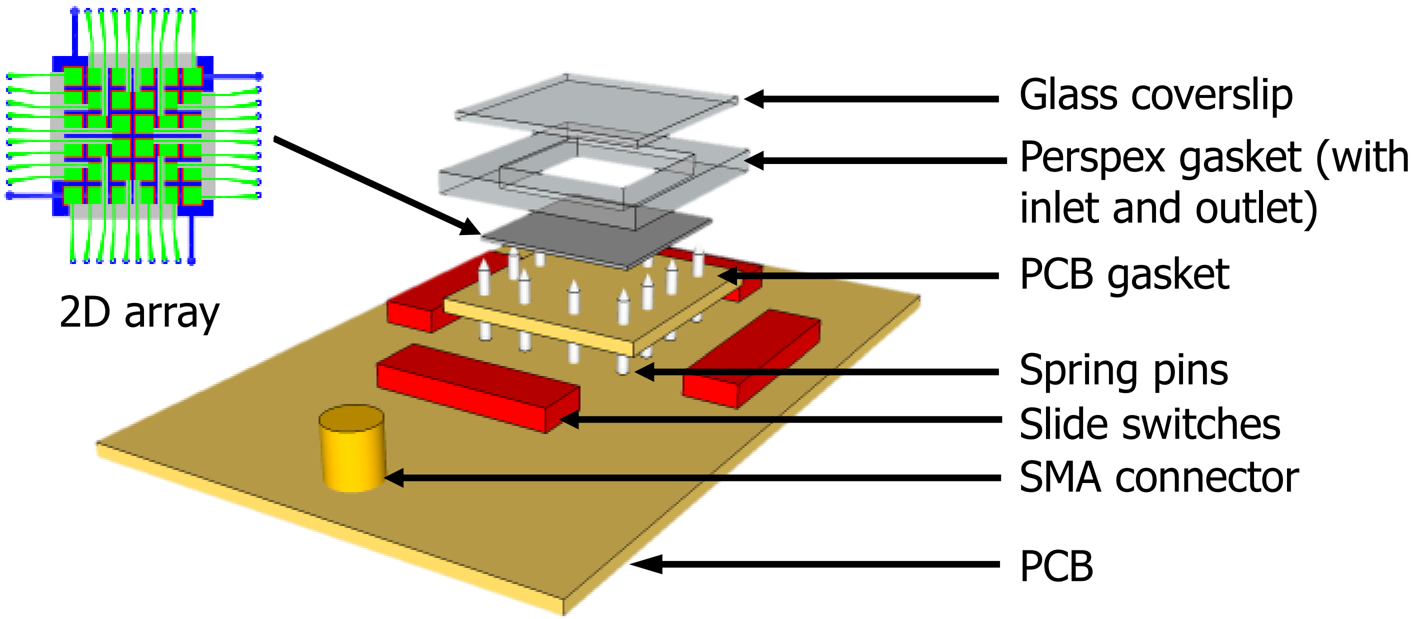
- Optical (**observation**) from above
- **Fluidic** interface still to be engineered
  - Basis in microscale silicon substrate will require further development
- **Electronic interface** achieved with a chip carrier

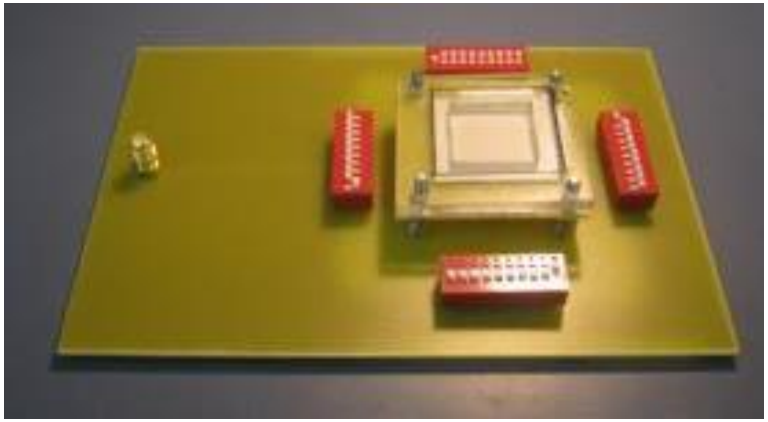


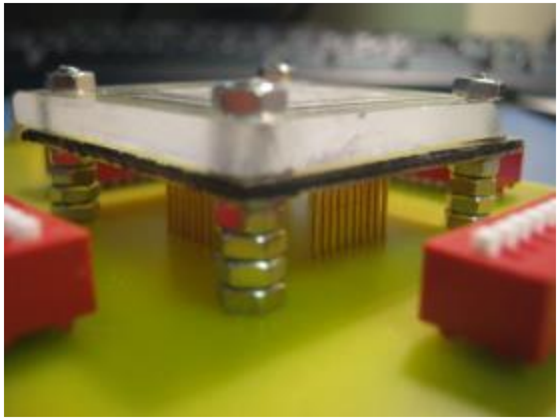




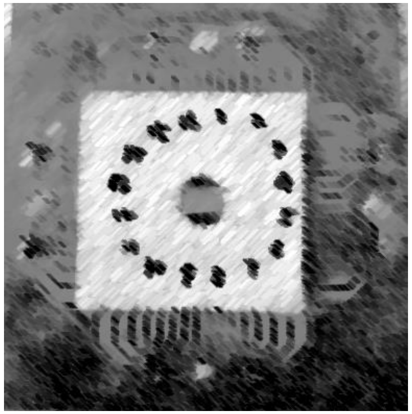
Example: Thick Film Sonotweezer







Summary



Summary

- Sonotweezers development is **bifurcated**
  - **Simple devices** subject to *ad hoc* development
    - **Not** covered here
  - **Multielement devices** requiring specialised fabrication
- Three main components
  - **Sonotweezer** itself
    - Based on micromachined piezoelectrics
  - **Electronics**
  - **Ancillary hardware**
    - Requires **application specific** development
- PC also required for **control** in most systems
- **Many** future possibilities
  - Ultimate target is ultrasound equivalent of **spatial light modulator in optical tweezing**