TOSHIBA

Micro Manipulator Array for Nano-bioelectronics Era

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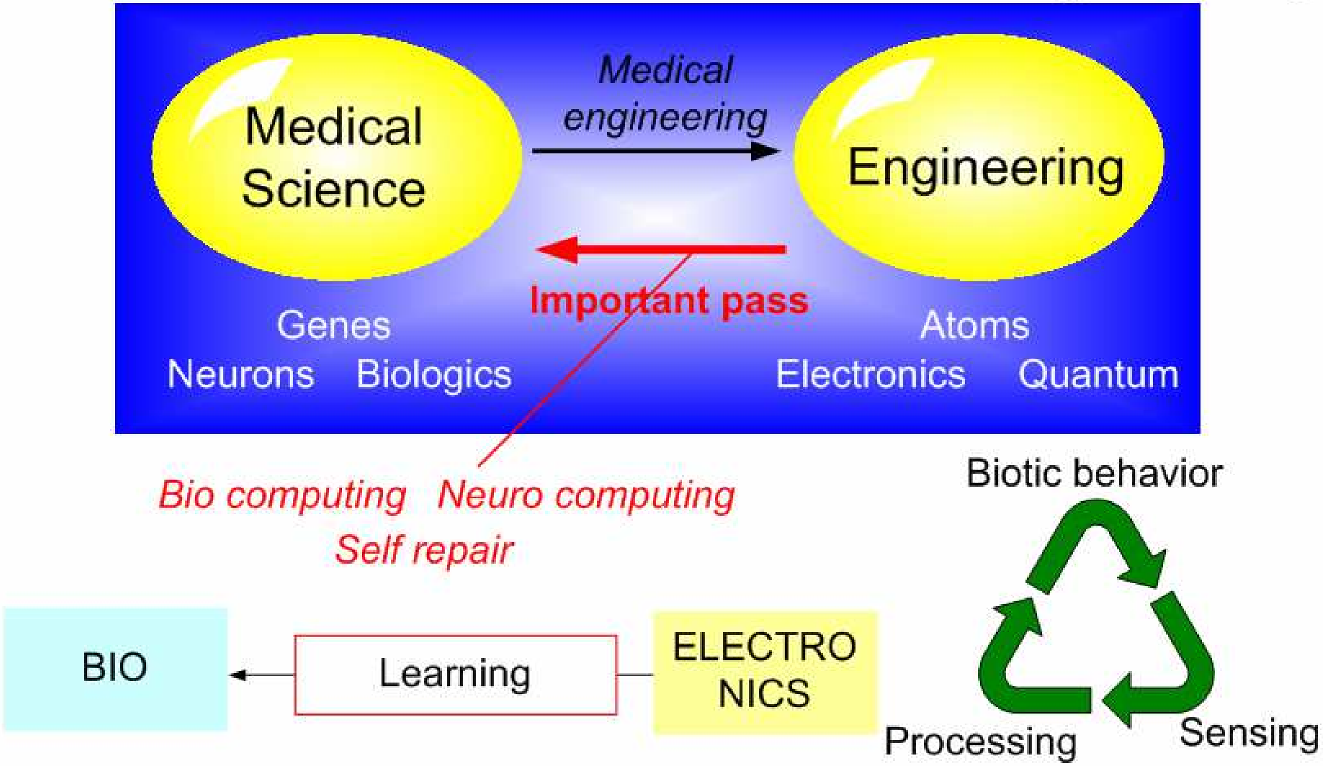
OUTLINE

- Introduction
- Device Structure
- Physical Interaction
- Experiments & Results
- Future Visions
- Summary

MOTIVATION

Fusion between medical science & engineering



Self-Repair and Supplemental Functionality - The ability for biological organs and organisms to function even though some cells have been damaged.

THE APPROACH

Applied field of nanotechnology

Resources & Energy

Communications & Electronics

Biotechnology

Medical care & Health care

Chemical → Application for next generation medical care

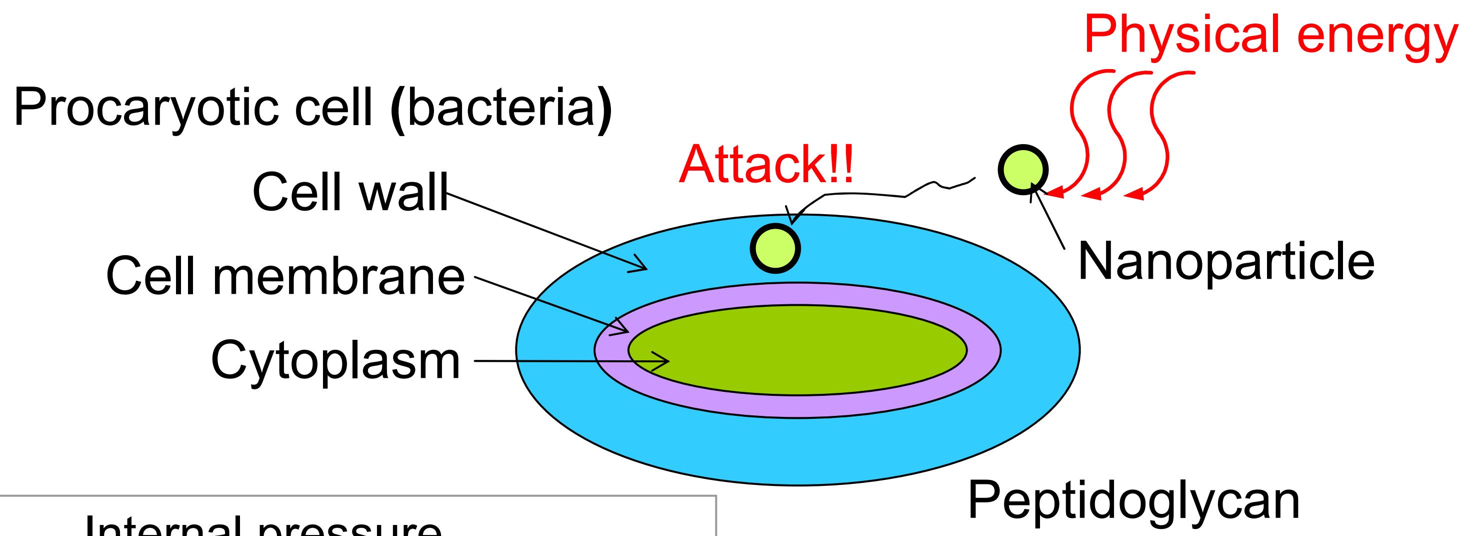
Diagnosis	Treatment
Micro-TAS	DDS
DNA chip	

Physical → Physical Antibiotics

Approach as electronics company

This leads to the promising future technology of "tailor-made medical treatments" corresponding to the needs of the individual.

PHYSICAL ANTIBIOTICS

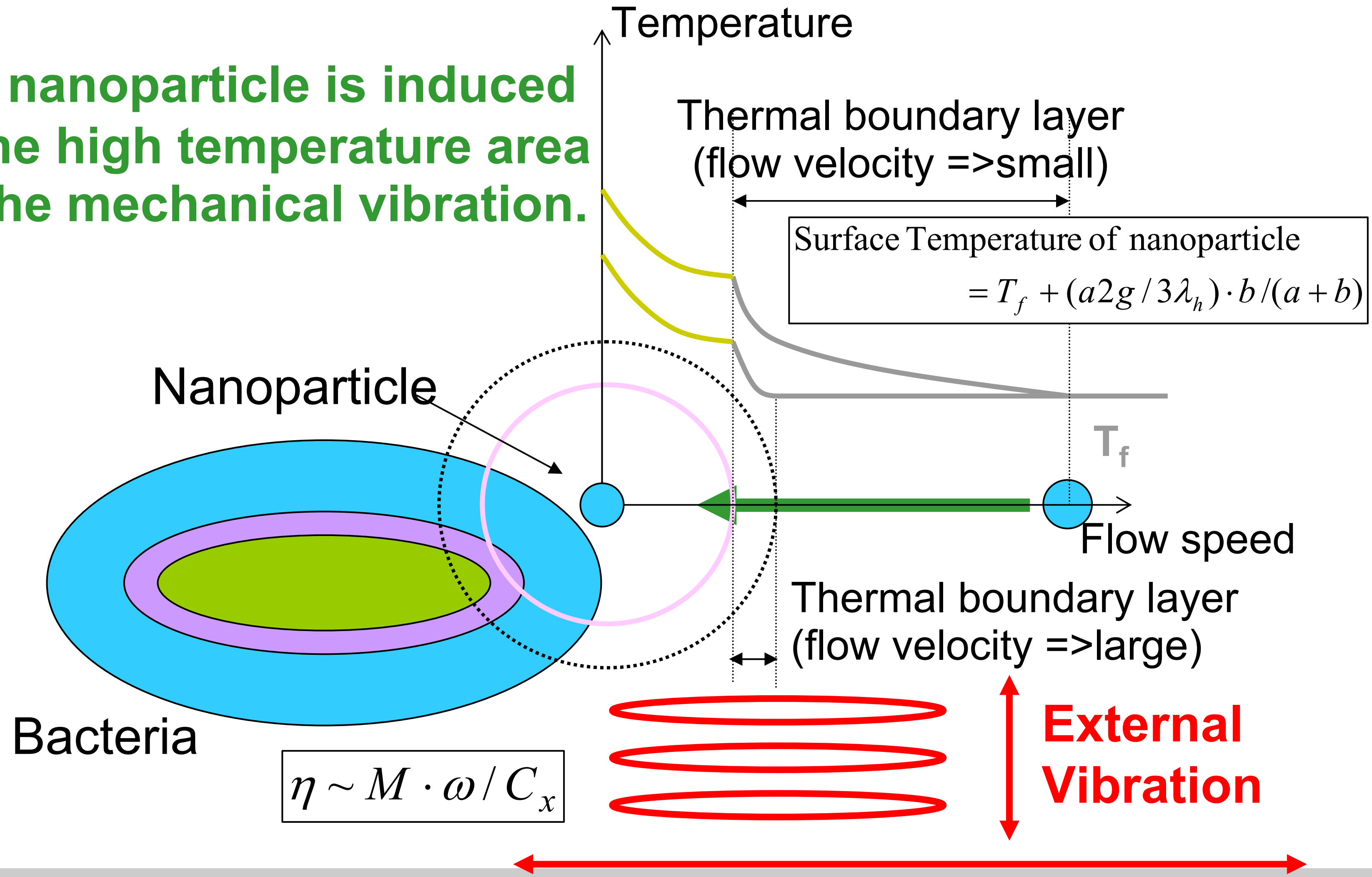


Internal pressure	
Gram-positive anaerobic	20Pa
Gram-negative anaerobic	8Pa

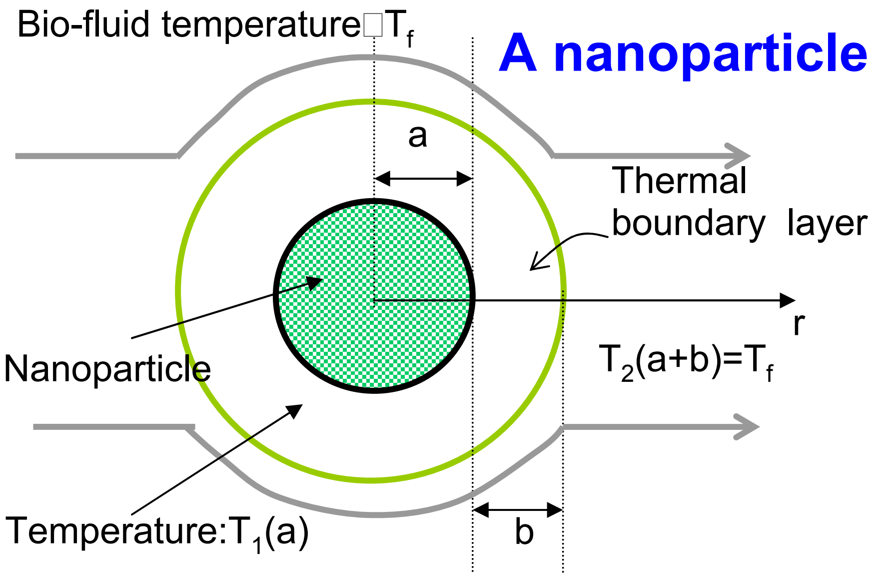
Mechanical vibration where a high surface temperature is obtained by the thermal boundary theory is one method by which nanoparticles can be introduced.

ADSORPTION OF NANOPARTICLES

The nanoparticle is induced to the high temperature area by the mechanical vibration.



ADSORPTION OF NANOPARTICLES



A nanoparticle in spherical coordinates

$$T_1(r) = A/r + B, \quad 0 < r < a \qquad (1)$$

$$T_2(r) = C/r + D, \quad a < r < a + b \qquad (2)$$

$$-\lambda_a (dT_1/dr)_{r=a} \cdot 4\pi a^2 = 4\pi a^3 \cdot g/3 \qquad (3)$$

$$-\lambda_h (dT_2/dr)_{r=a} \cdot 4\pi a^2 = 4\pi a^3 \cdot g/3 \qquad (4)$$

$$T_2(a+b) = T_f \qquad (5)$$

$$T_1(a) = T_2(a) \qquad (6)$$

$$T_1(a) = T_f + (a^2 g/3\lambda_h) \cdot b/(a+b) \qquad (7)$$

Parameters

$T_1(r)$: Thermal distribution (nanoparticles)

$T_2(r)$: Thermal distribution (stagnant layer)

a: Radius of the nanoparticles

b: Width of the stagnant layer

λ_a: Thermal conductivity (nanoparticles)

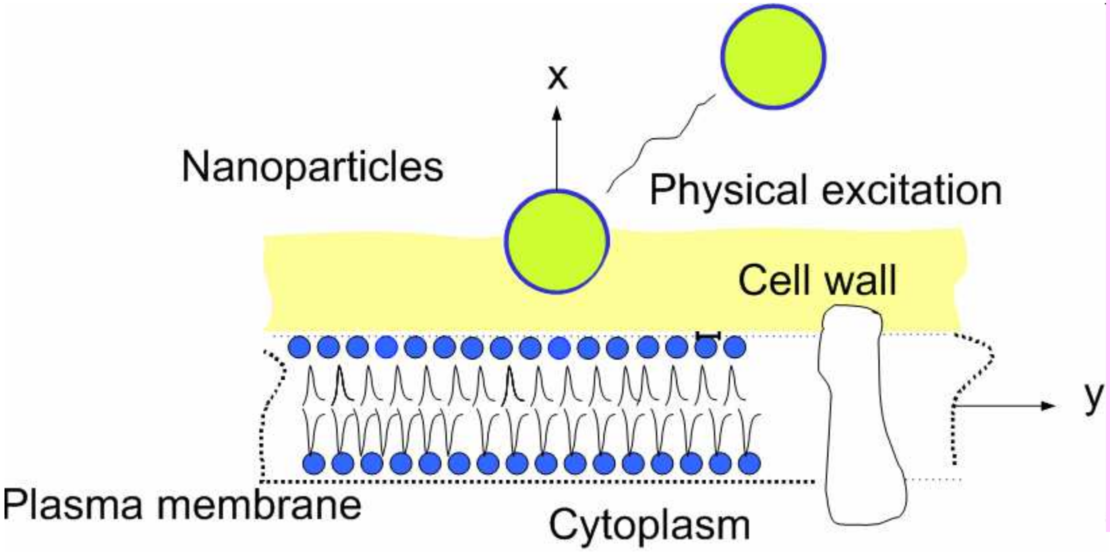
λ_b: Thermal conductivity (biofluid)

g: Energy generation rate in the nanoparticles

T_f: Flow temperature of the biofluid

$T_1(a)$: Surface temperature of the nanoparticles

VIBRATION EFFICIENCY



$$M \cdot x'' = -C_x (x' - y') \quad (1)$$

$$M \cdot \Delta x'' + C_x \cdot \Delta x' = -M \cdot y'' \quad (2)$$

$$\Delta x = A \cdot e^{j\omega t} \quad (3)$$

$$y = B \cdot e^{j\omega t} \quad (4)$$

$$(C_x / M \cdot \omega)^2 = \eta^{-2} - 1 \quad (5)$$

$$C_x = k_B T / D \quad (6)$$

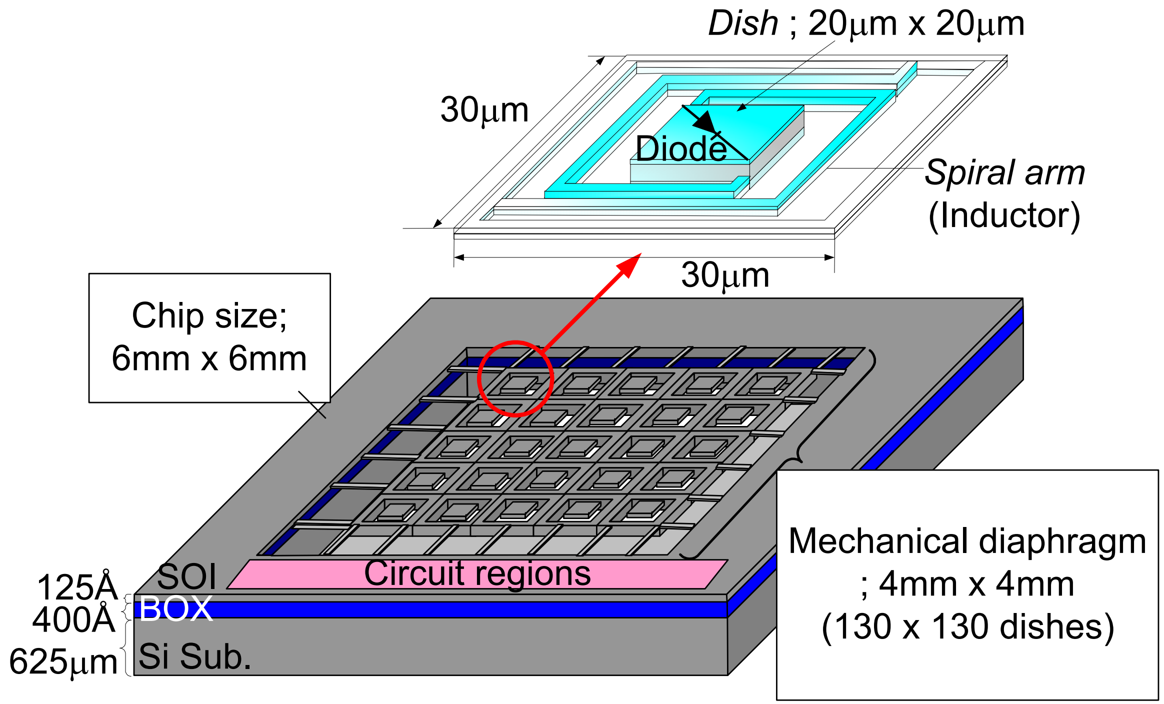
$$\eta \sim M \cdot \omega / C_x \quad (7)$$

Indicator for designing the in vivo and In vitro applications.

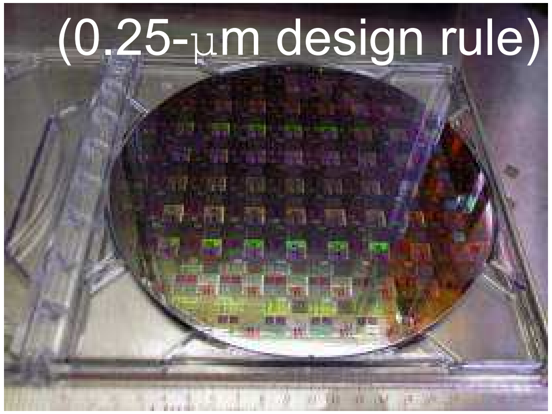
Parameters

M: Motion for a mobile protein with mass
C_x: Viscous damping constant
ω: Angular frequency of external mechanical vibration
η: Vibration efficiency as the ratio of the absolute value
D: Diffusion constant
k_B: Boltzmann constant
T: Absolute temperature

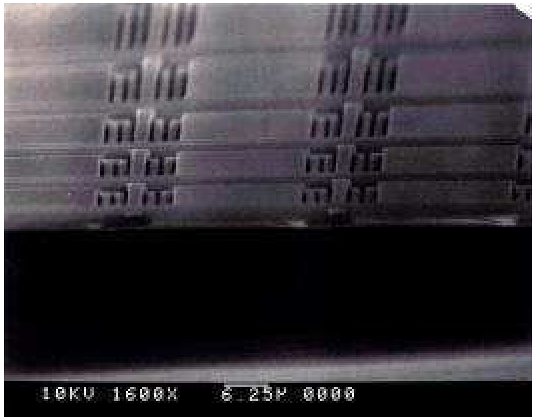
DEVICE STRUCTURE



8-inch SOI wafer
(0.25-μm design rule)



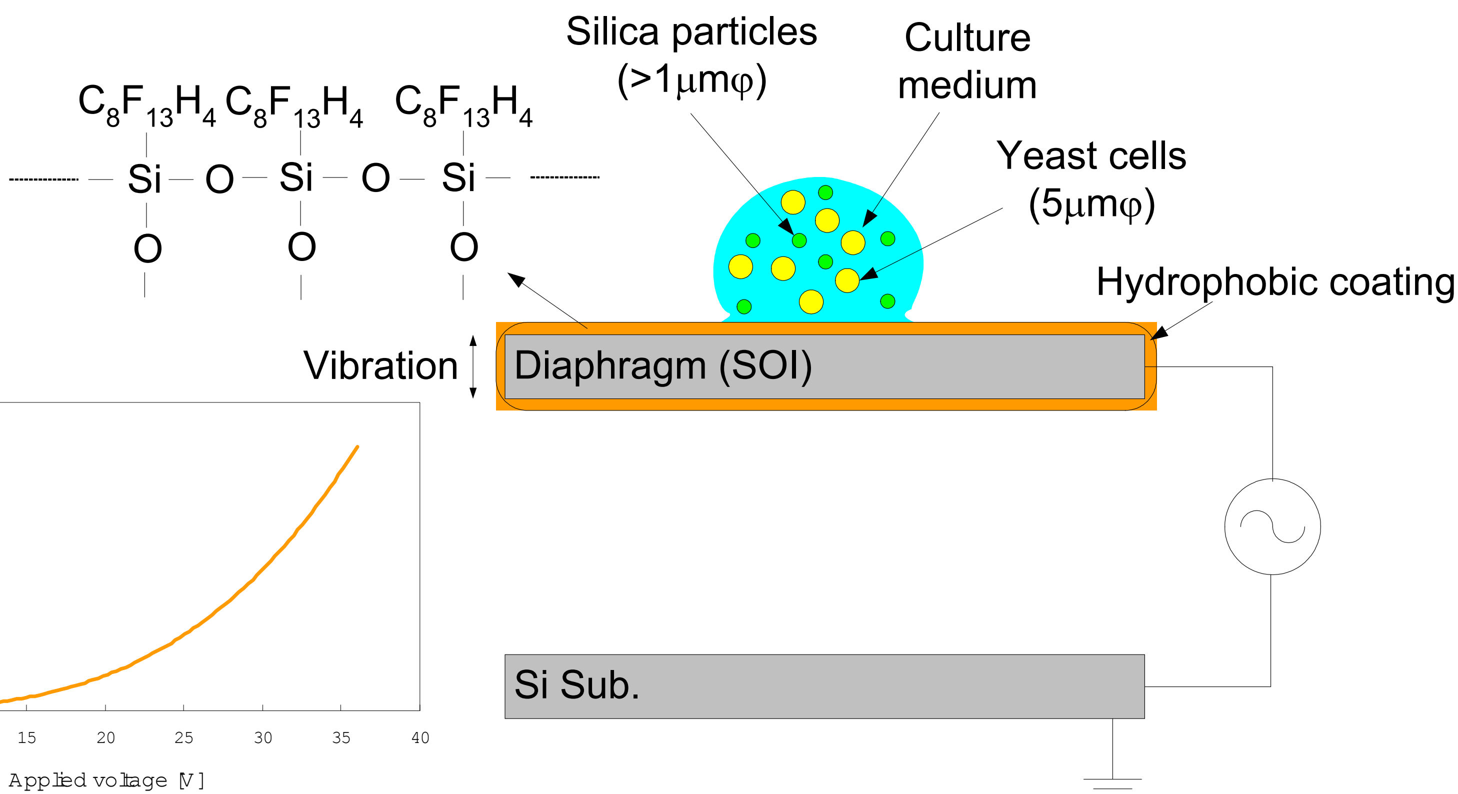
CMOS+MEMS process

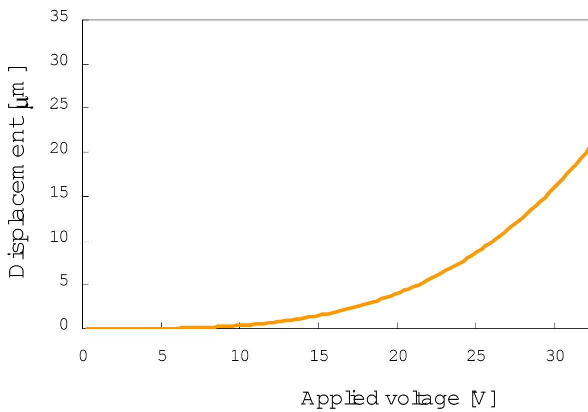


Mechanical diaphragm
(SEM image)

- **Collision energy =>Vibrating**
- Electric heating energy =>Joule heating

ELECTROSTATIC VIBRATING





Yeast cells are chosen for testing material since they have similar characteristics to typical bio-cells.

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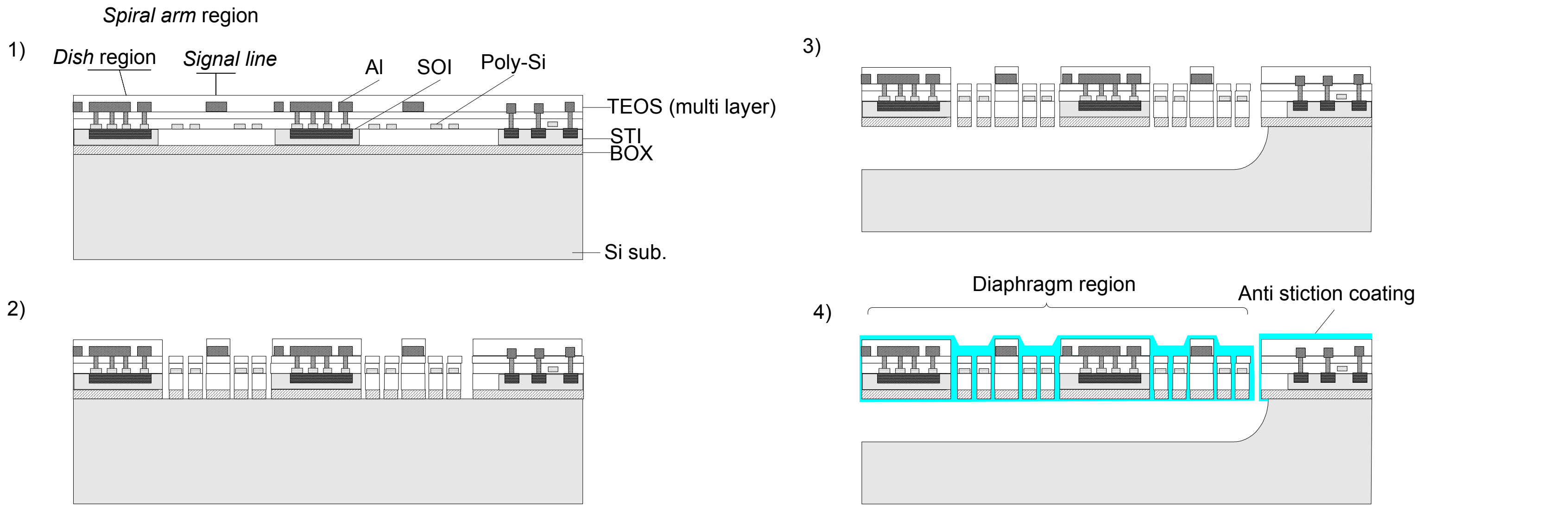
FABRICATION PROCESS



(1) The *micro dish* and *spiral arms* are fabricated by CMOS processing (0.25-µm design rule).

(2) The TEOS layer is etched down to the silicon substrate by RIE, and the formed lattice is neatly arranged in a 30-µm pitch.

(3) A cavity is formed by isotropicly etching the silicon substrate using XeF_2 gas.

(4) A hydrophobic coating is deposited using $C_8F_{13}H_4SiCl_3$ and H_2O gases.

INTERACTION BETWEEN CELLS & PARTICLES

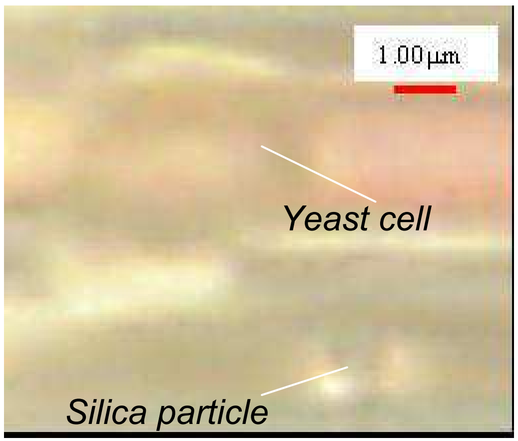
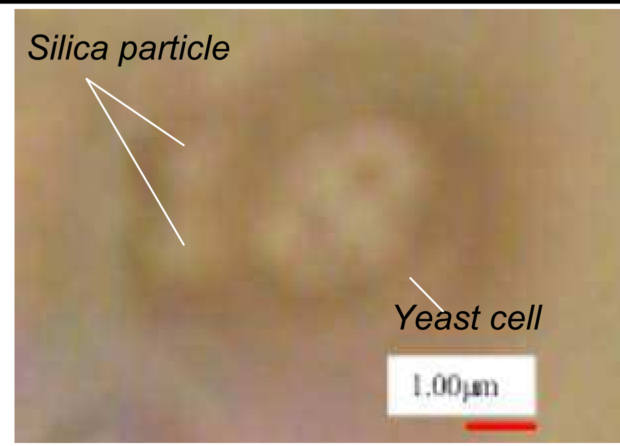
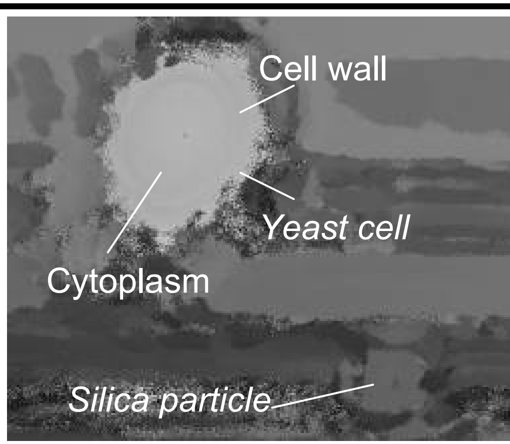
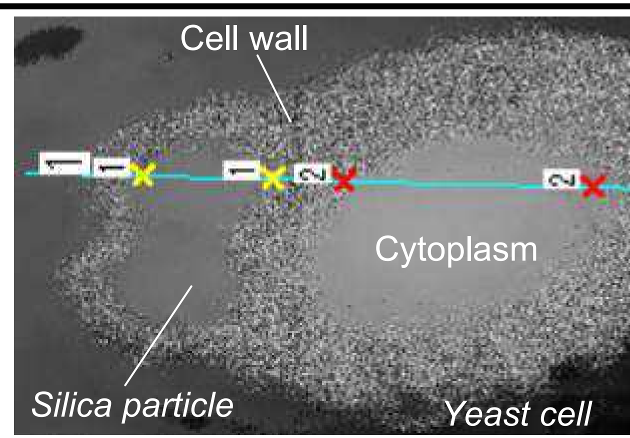
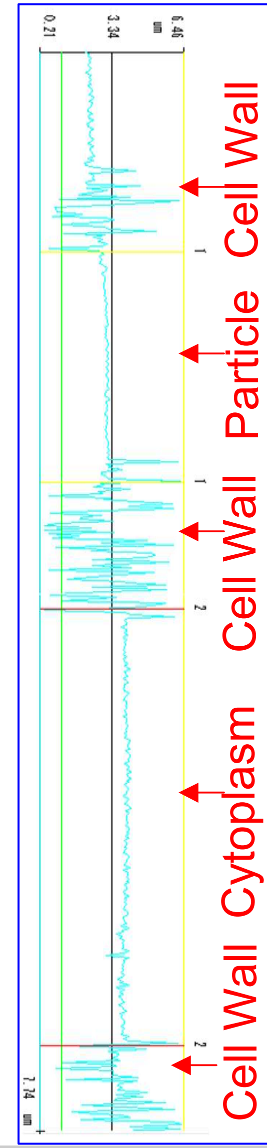
	Yeast cell & Silica particle	After excitation (30V 1kHz signal)
Optical microscope		
Laser microscope		

Image 1 (optical microscope, yeast cell & silica particle):

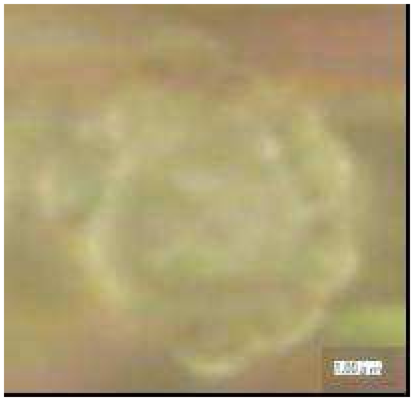
Image 2 (optical microscope, after excitation):

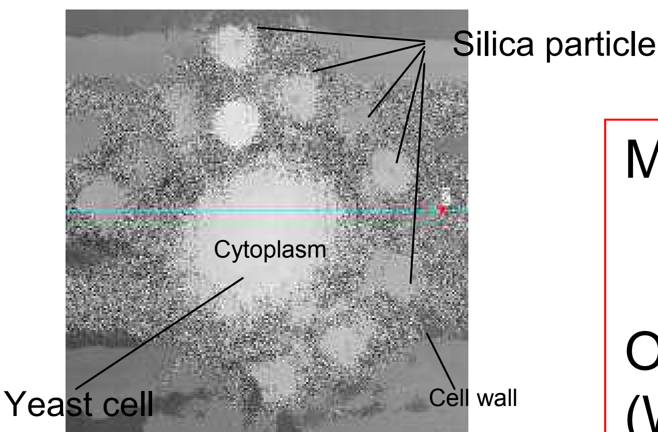
Image 3 (laser microscope, yeast cell & silica particle):

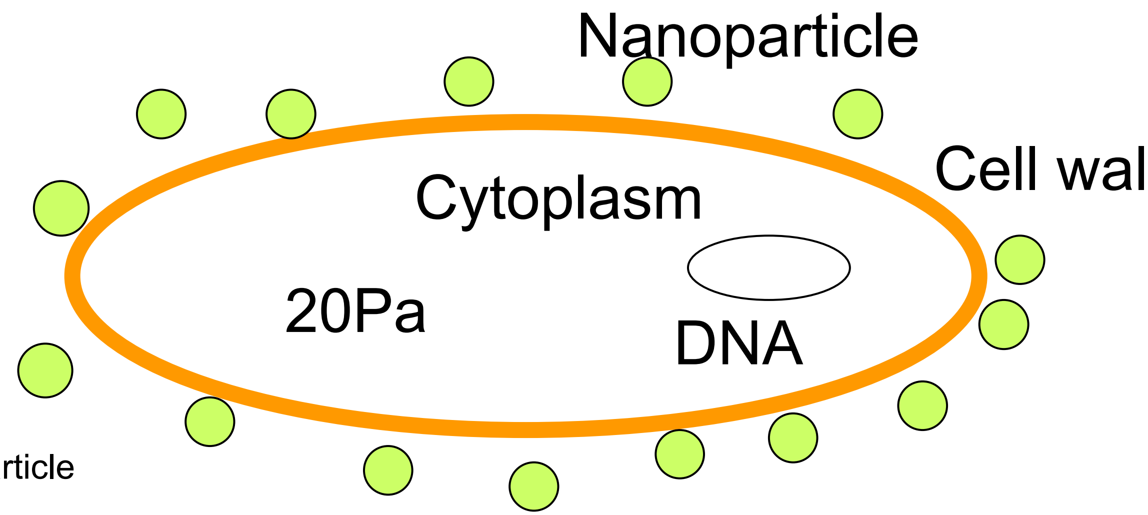
Image 4 (laser microscope, after excitation):



HEATING OF HIGH-PRESSURE CYTOPLASM USING GROUPS OF NANOPARTICLES





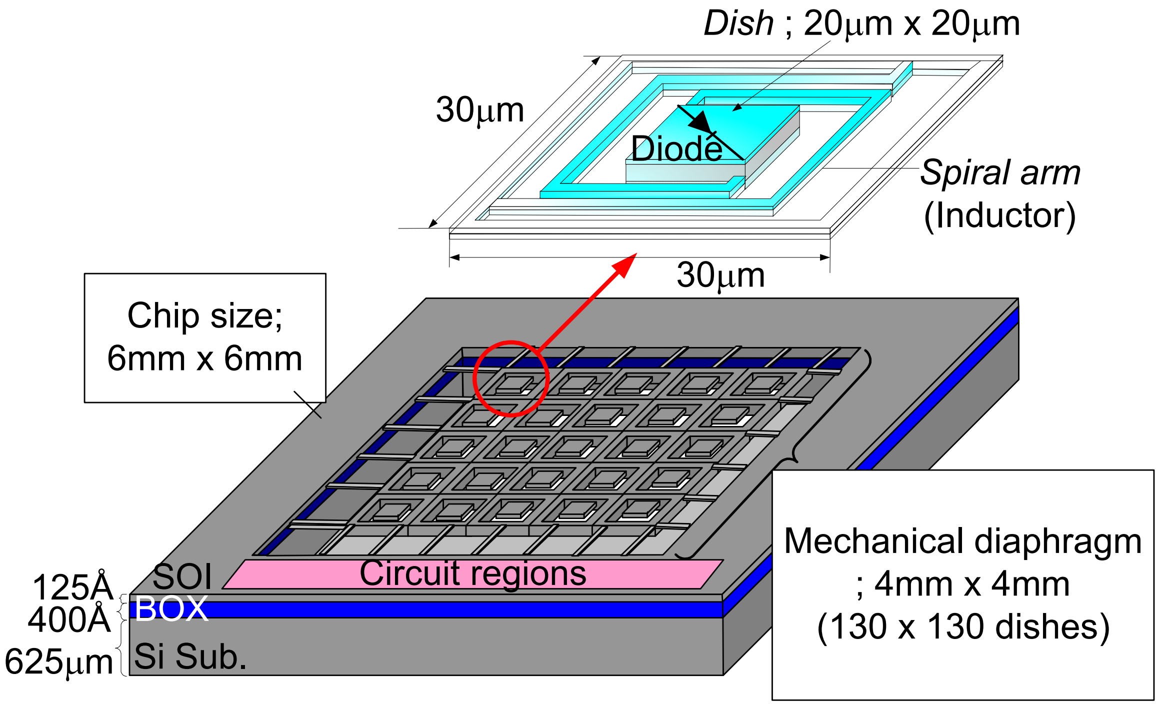


Molar elevation of boiling point

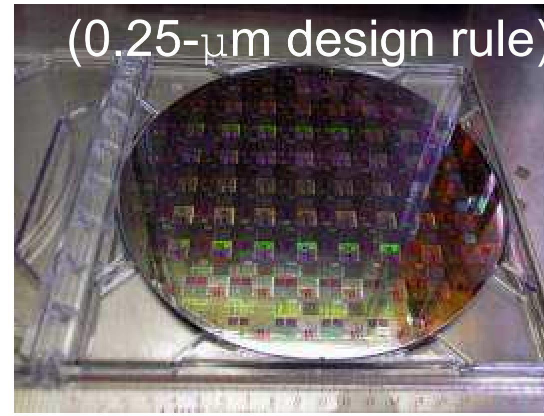
: sterilization temperature 150~200ºC

Osmotic pressure : P=k*C*T [mol/l] [k]
(W.Pfeffer)

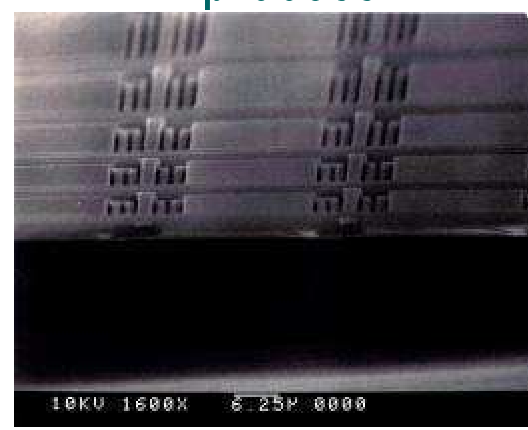
DEVICE STRUCTURE



8-inch SOI wafer
(0.25-μm design rule)



CMOS+MEMS process



Mechanical diaphragm
(SEM image)

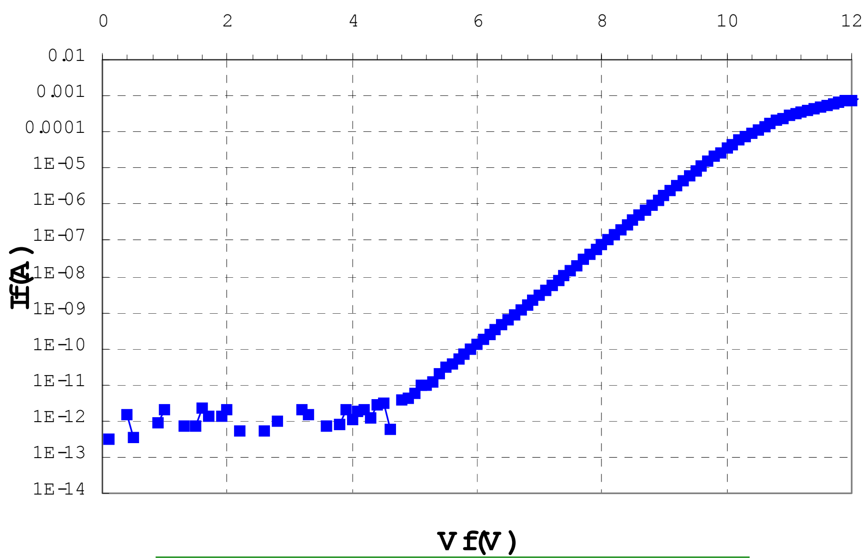
- Collision energy =>Vibrating
- **Electric heating energy =>Joule heating**

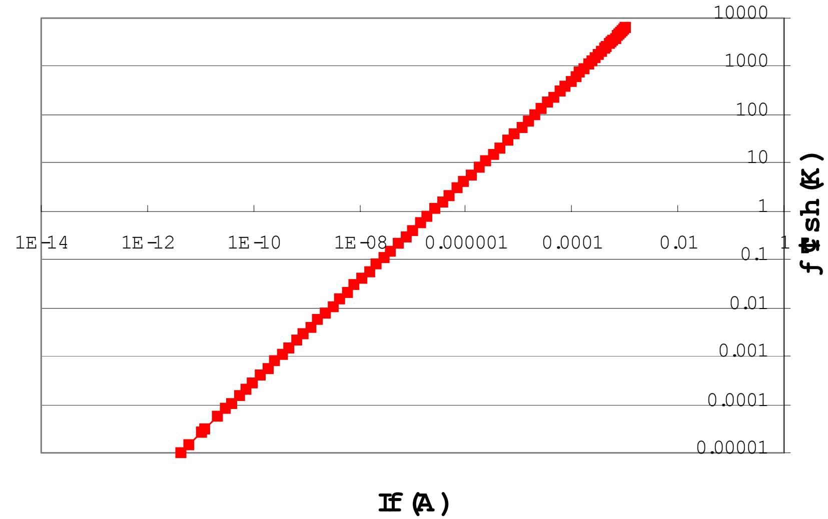
LOCAL HEATING AT MICRO DISH

I-V characteristic versus dish temperature

Temperature increase of the micro dish versus If

(In atmosphere)



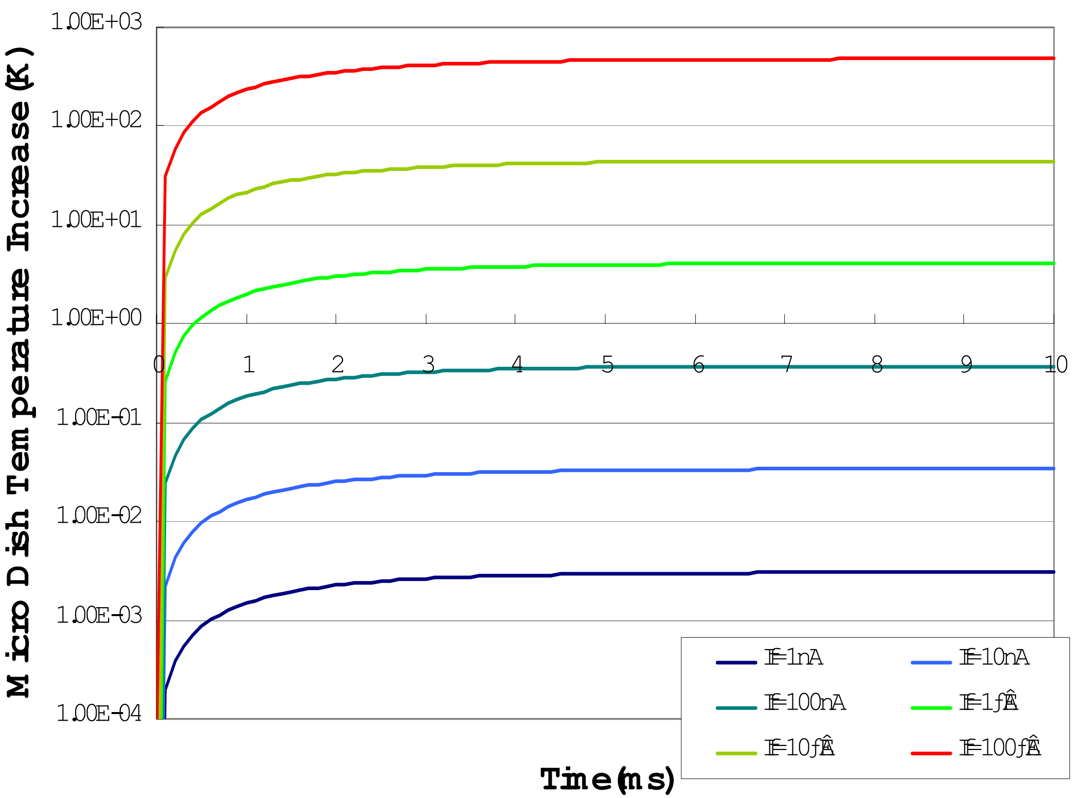


G_{th} :2.0E-6 (W/K)

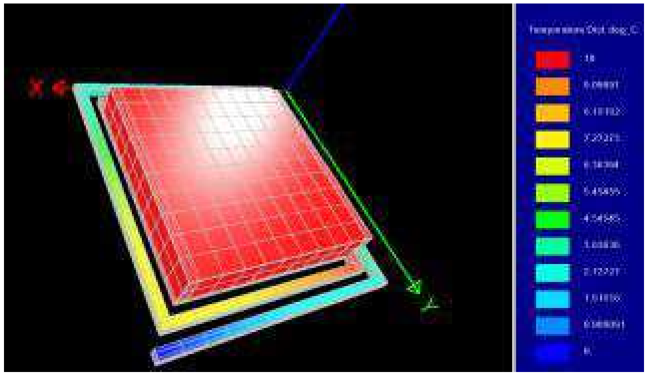
C_{th} : 3.0E-9 (J/K)

$$\Delta T = \frac{Vf \cdot If}{G_{th}}\{1 - \exp(-tG_{th}/C_{th})\}$$

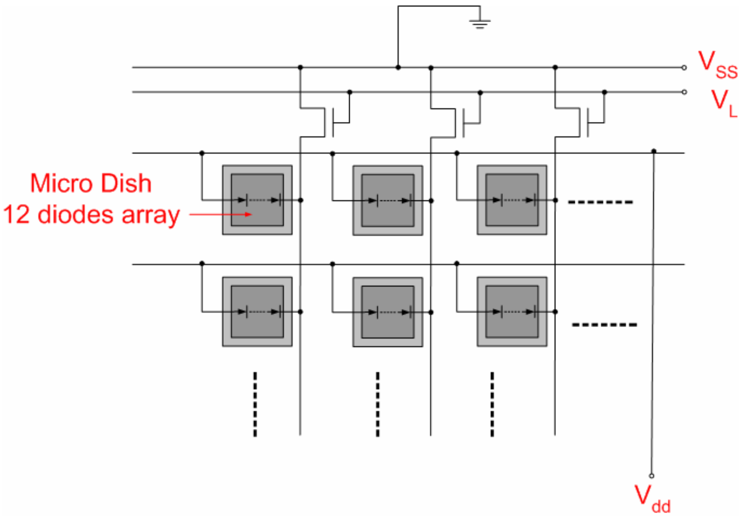
TURN ON CHARACTERISTICS

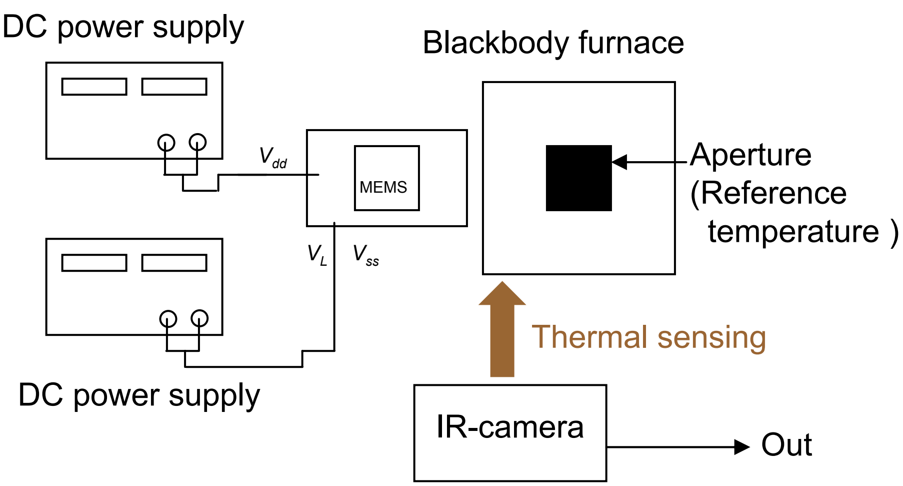


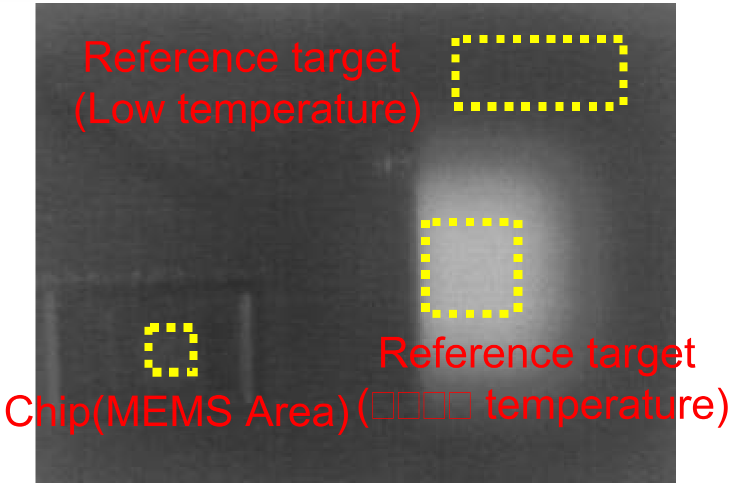
Thermic effect
of micro dish (10ºC)
by FEM

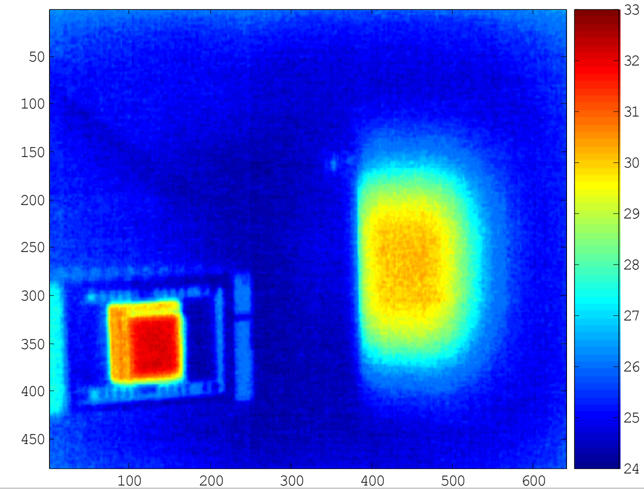


HEATING EXPERIMENT I.

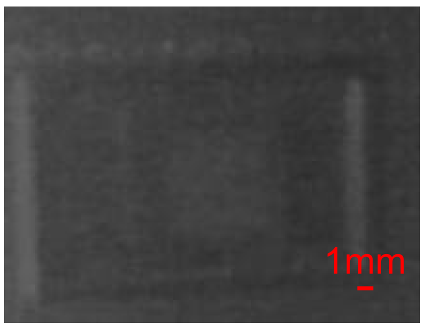
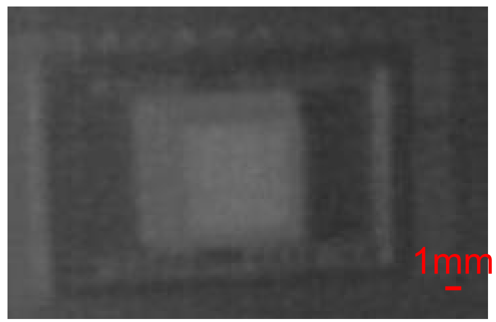
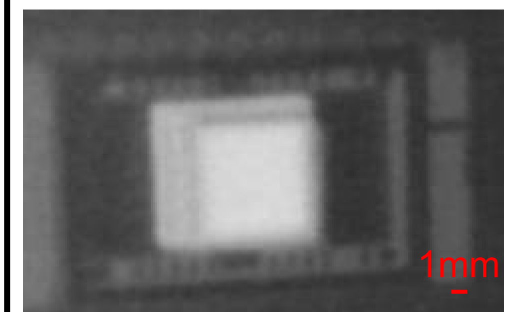
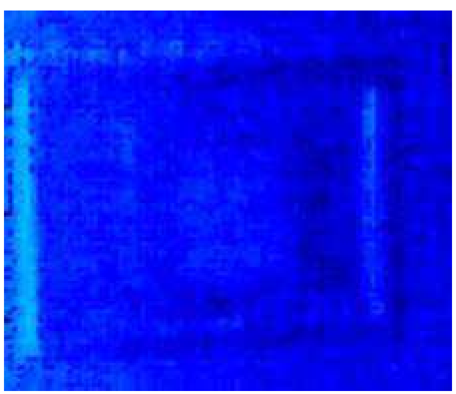
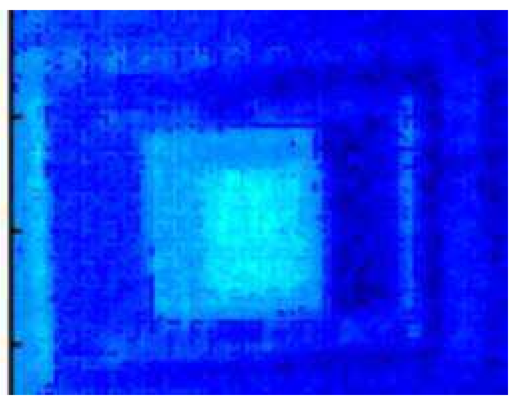
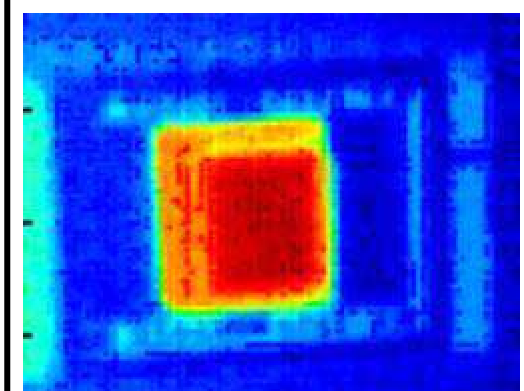




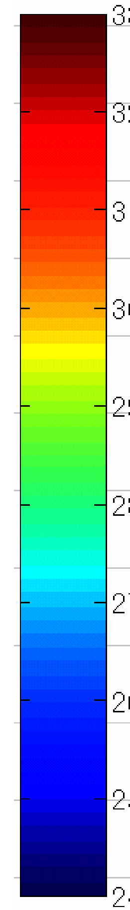




HEATING EXPERIMENT RESULTS I.

	□ V_L 0V	□ V_L 1.5V	□ V_L 2.0V
IR camera image			
Heat distribution analyze			

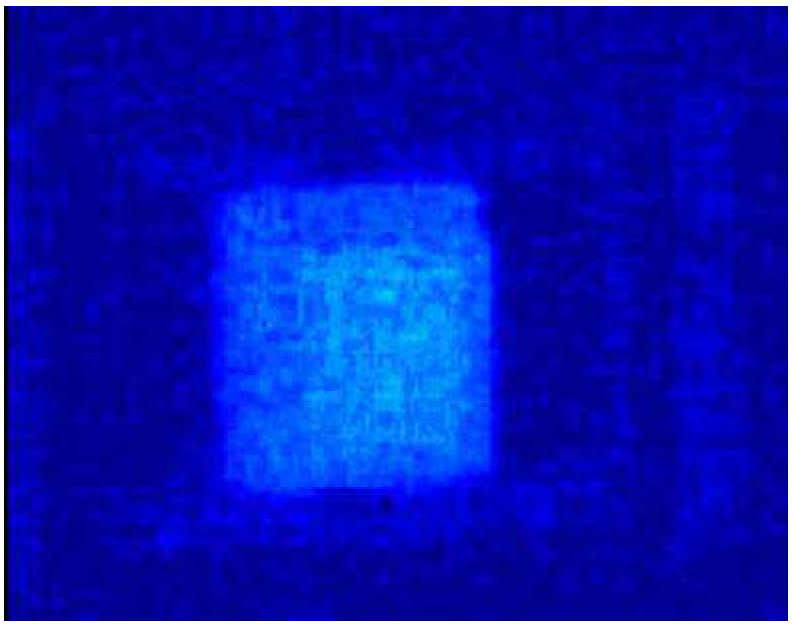
ºC



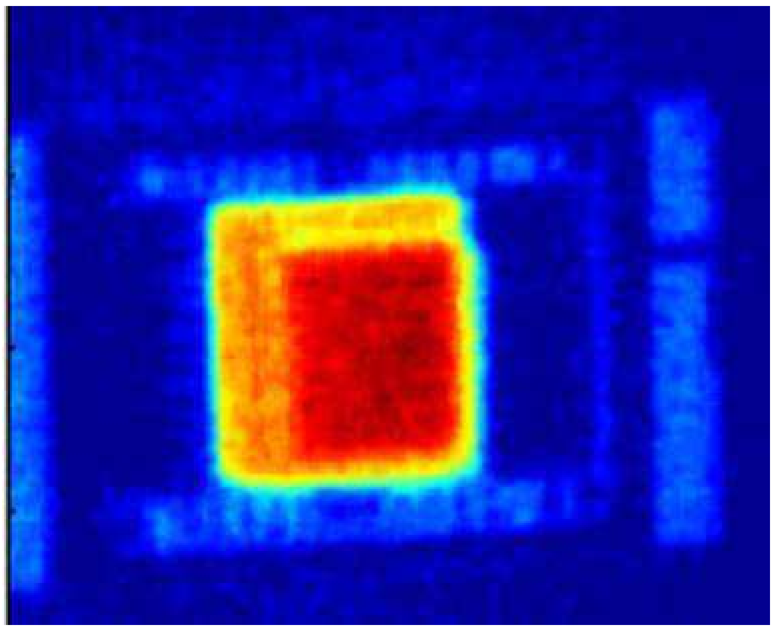
HEATING EXPERIMENT RESULTS I.

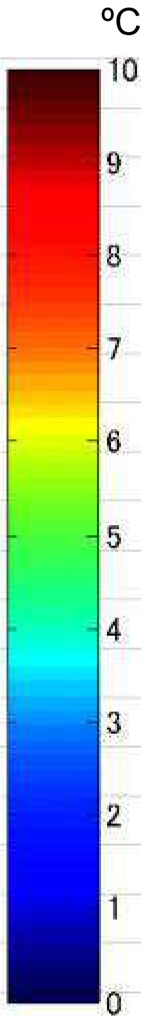
-Thermal difference-

□ - □



□ - □

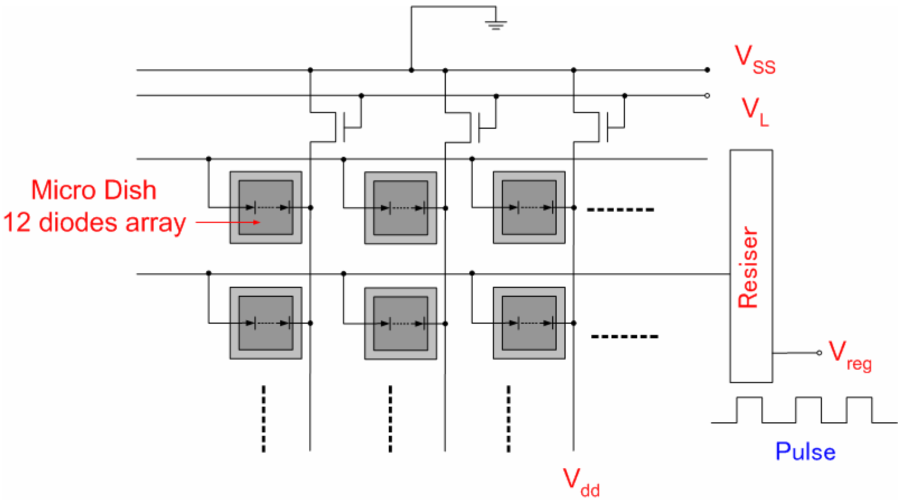




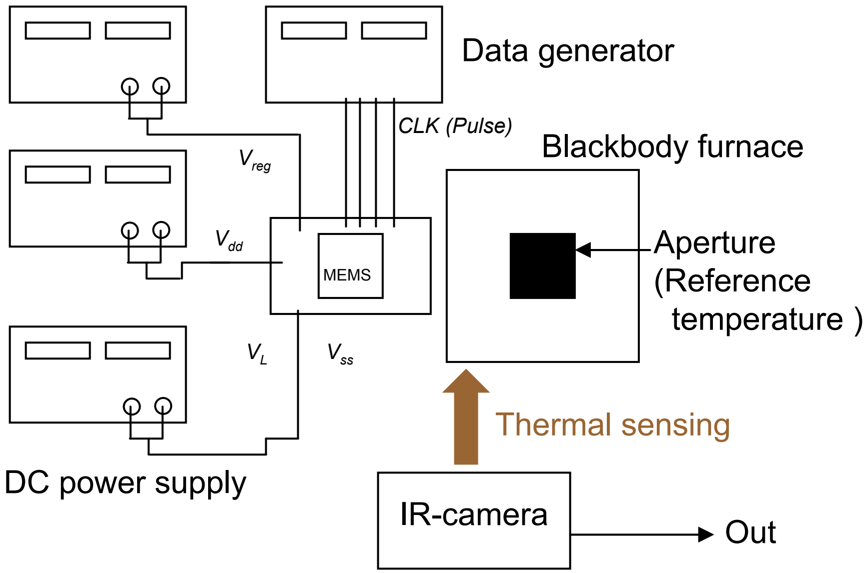
Heat effect : approx. 9.7 ºC

HEATING EXPERIMENT II.

Circuit configuration

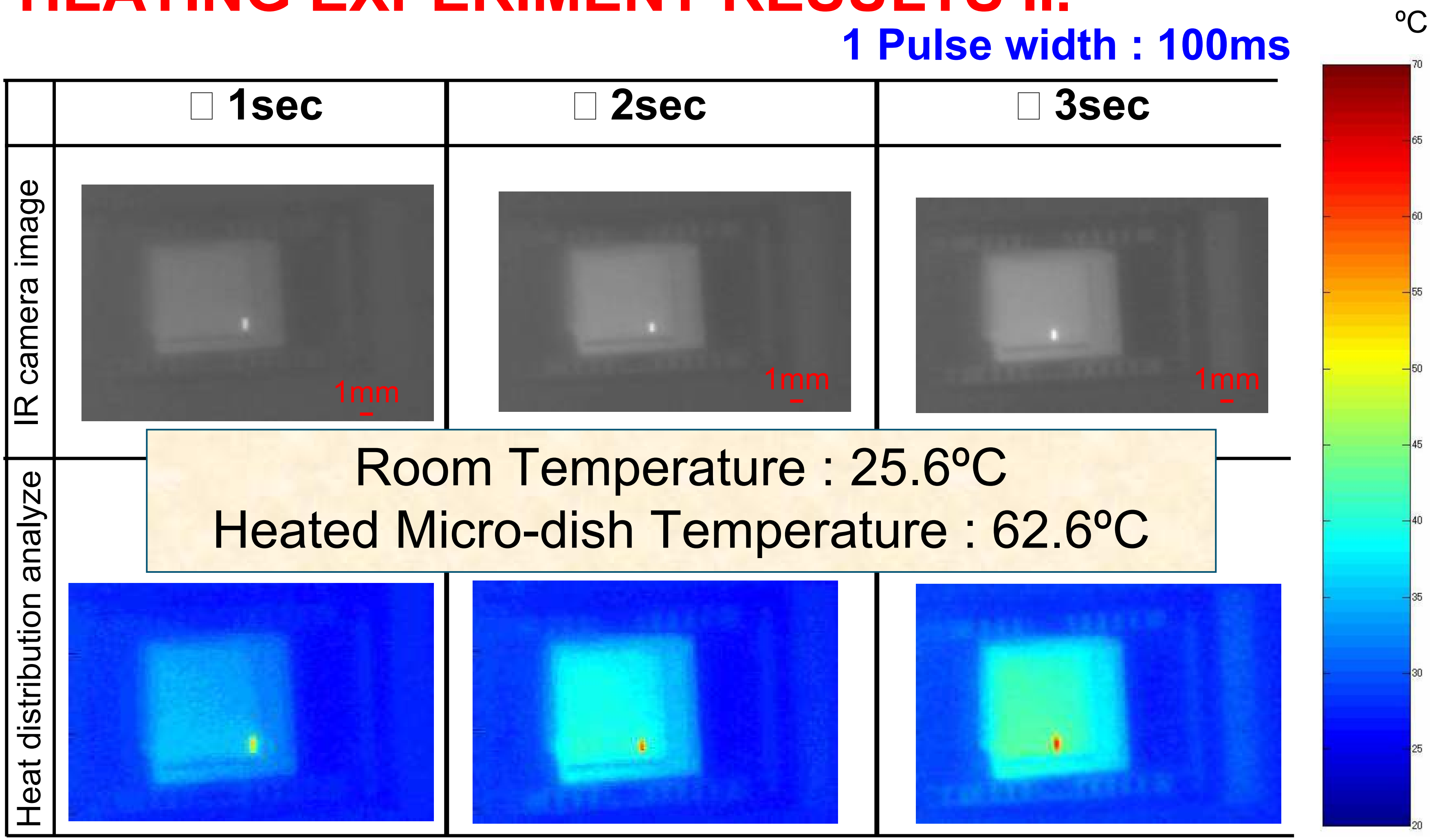


Measurement configuration



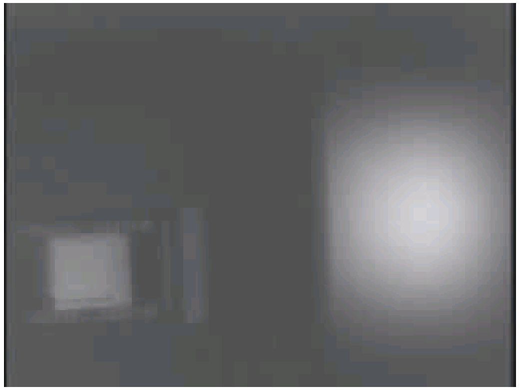
HEATING EXPERIMENT RESULTS II.

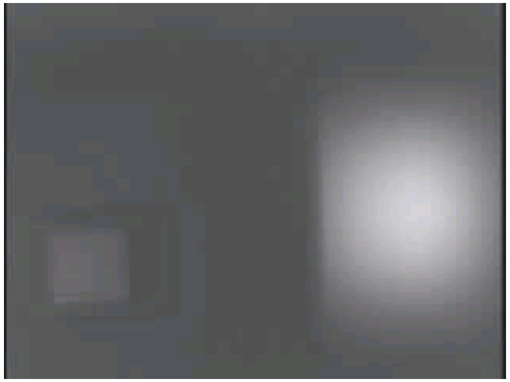
1 Pulse width : 100ms

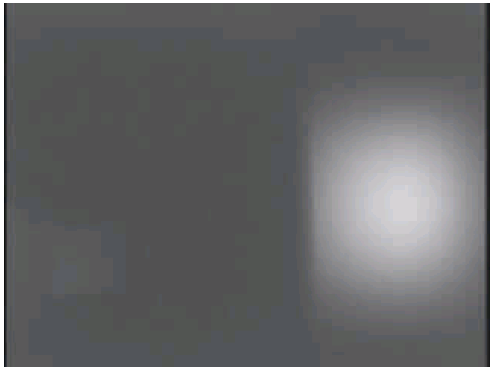


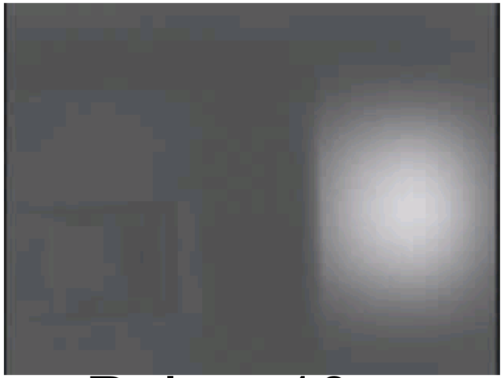
HEATING EXPERIMENT RESULTS II.

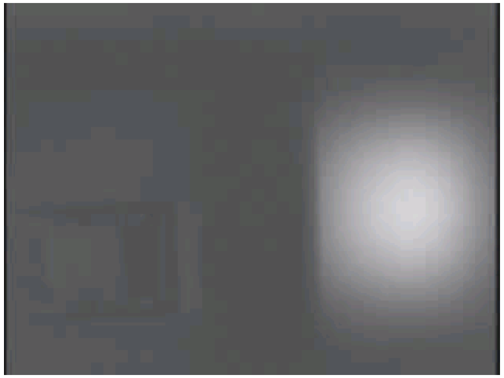
-Video movies-


Pulse: 1s

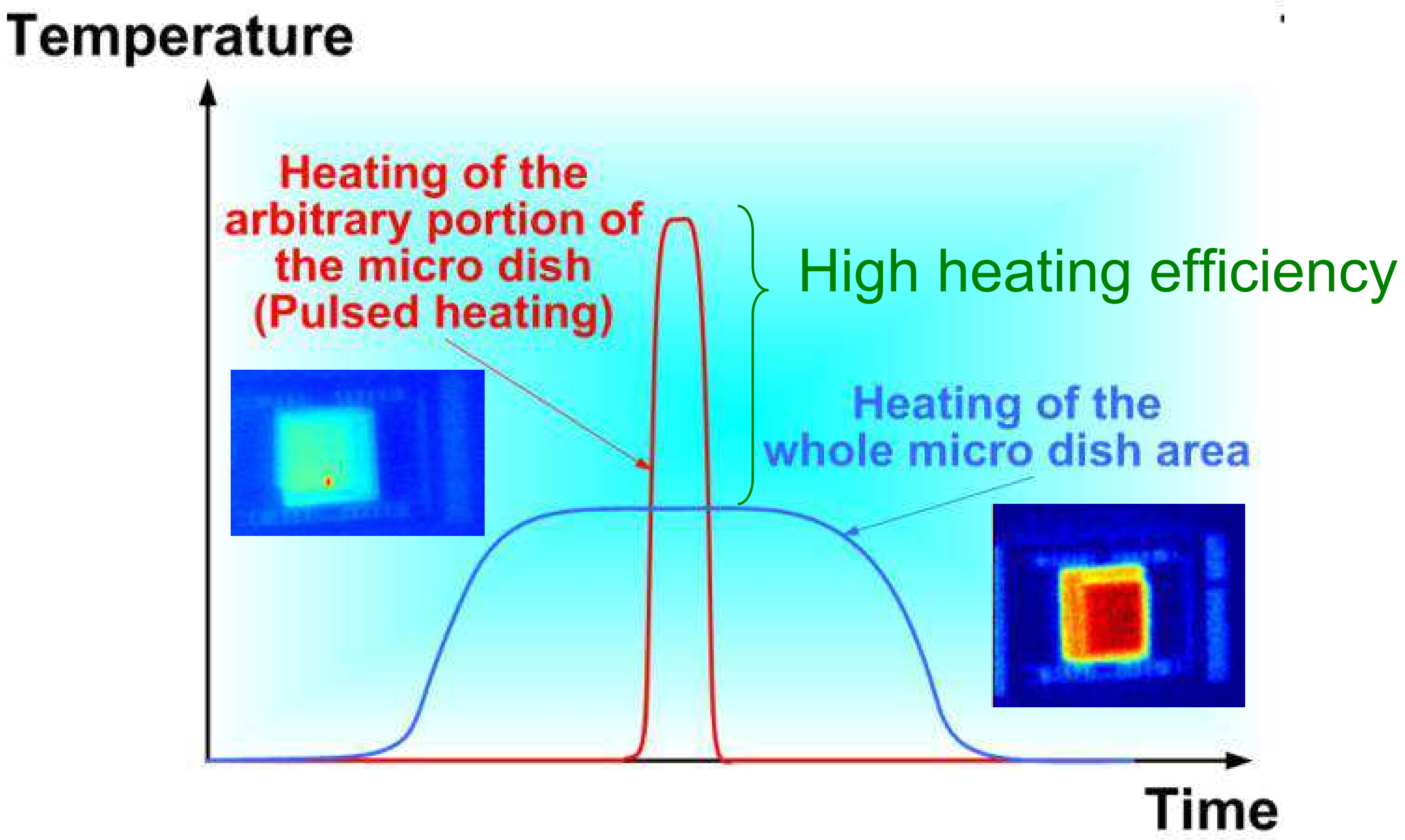

Pulse: 100ms


Pulse: 50ms


Pulse: 10ms


Pulse: 1ms

HEATING EFFECT COMPARISON



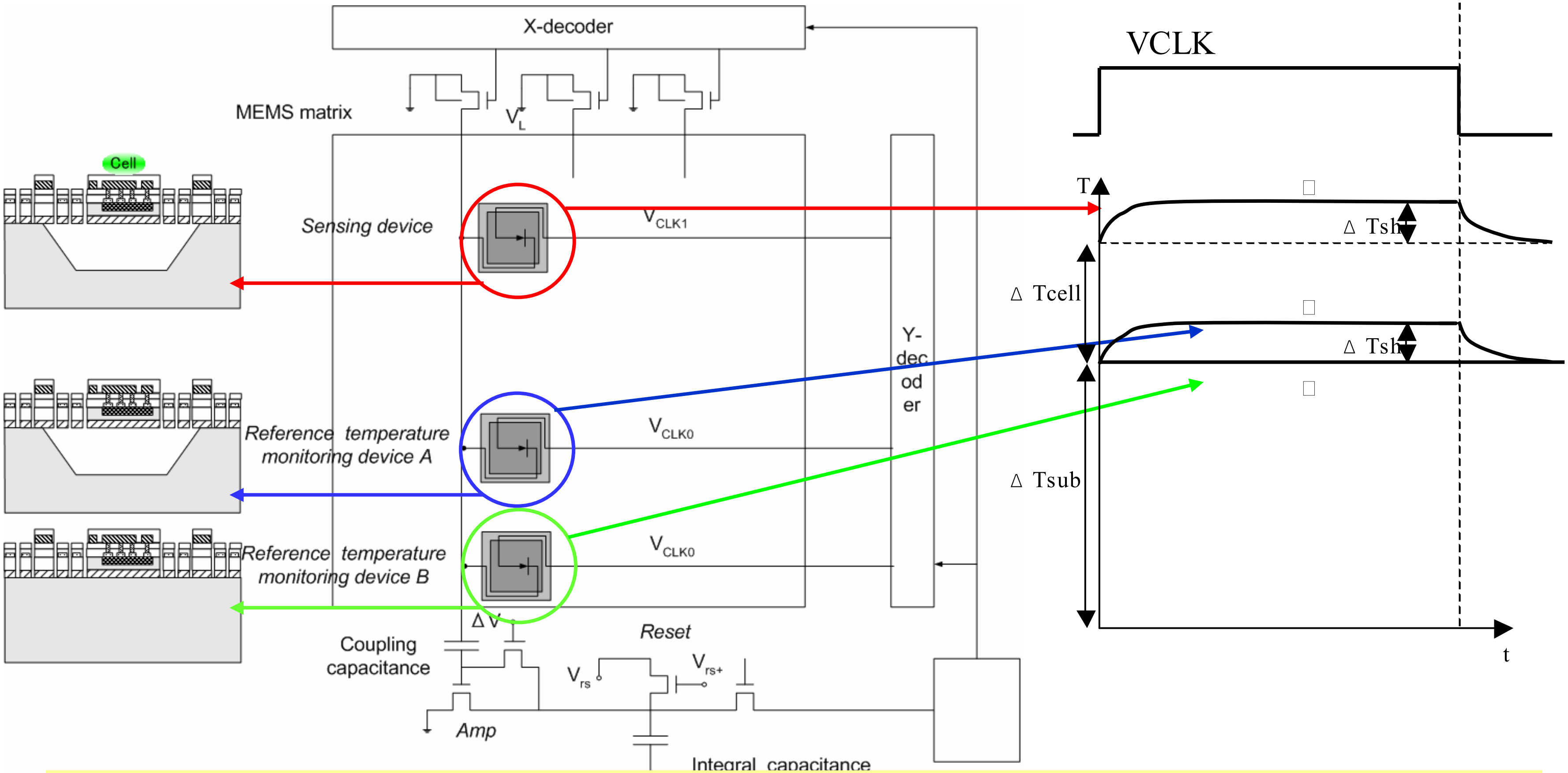
REMARKS (JOULE HEATING)

- ✓Heating of the whole micro dish array and just an arbitrary portion of the micro dish was demonstrated.

- ✓Rapid temperature switching on 'micro second' order was confirmed.

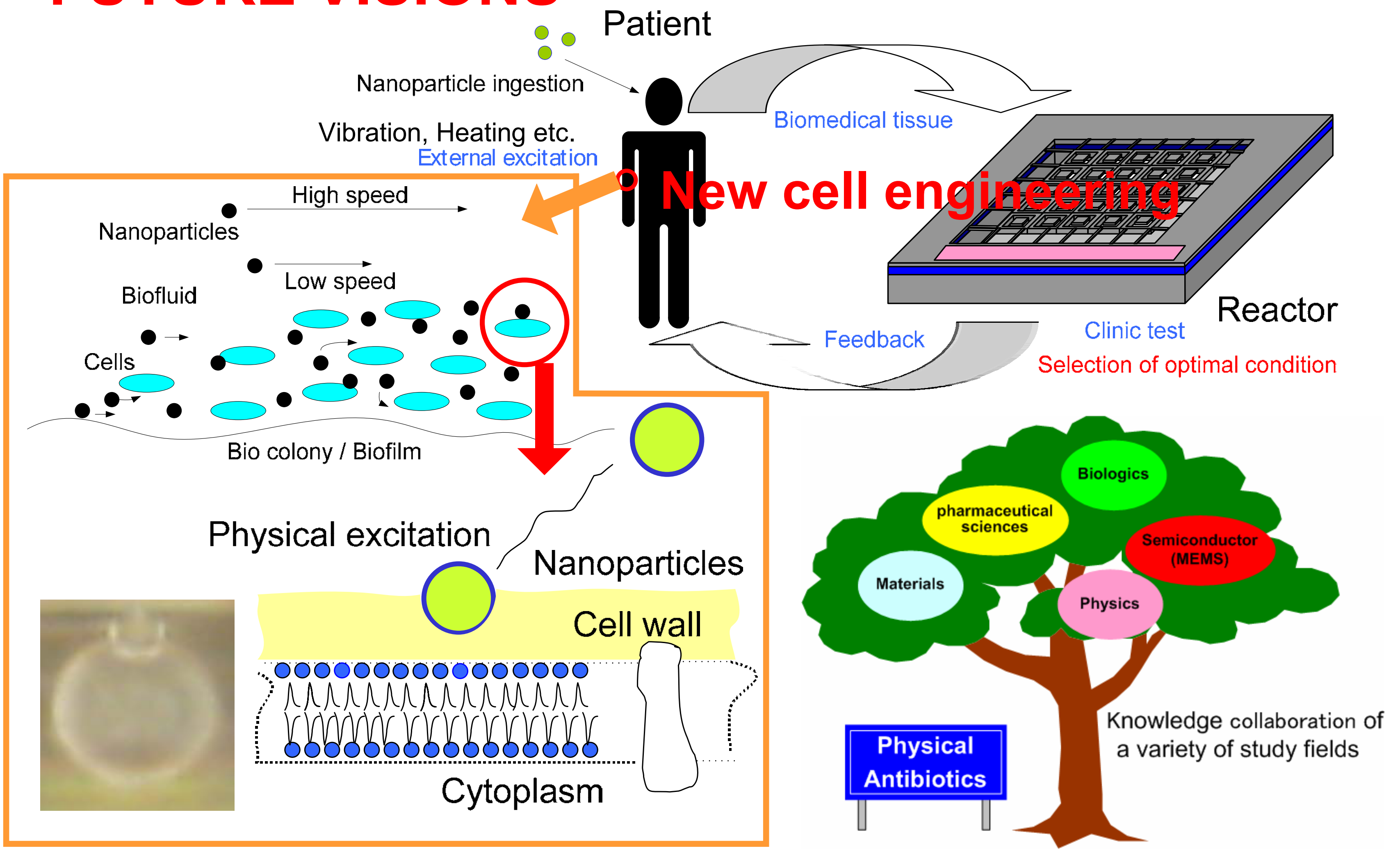
- ✓ More than twice the heat effect was achieved in heating an arbitrary portion compared with heating the whole micro dish.
(based on efficiency)

ADVANCED DEVICE



Exothermic biological reactions will cause temperature spikes in the vicinity of the reaction which in term causes the nearest diode to read a higher temperature. Scanning the array of temperature sensors across the chip will identify the particle X-Y position of the reaction.

FUTURE VISIONS



SUMMARY

- **We have developed a micro manipulator array using a novel MEMS-based structure.**
- **We also demonstrated direct physical control of the interaction between yeast cells and silica particles in liquid for the first time.**
- **The adsorption of the particle to the cell was demonstrated using vibrational energy, and Joule heating energy according to external excitation. These results show a potential impact in medical fields such as physical antibiotics and cell treatments and next generation bio-electronics schemes.**