JST-DFG Workshop on Nanoelectronics
5-7 March 2008 in Aachen

MEMS for Nano & Bio Technology

Hiroyuki Fujita
Center for International Research on MicroMechatronics
Institute of Industrial Science,
The University of Tokyo

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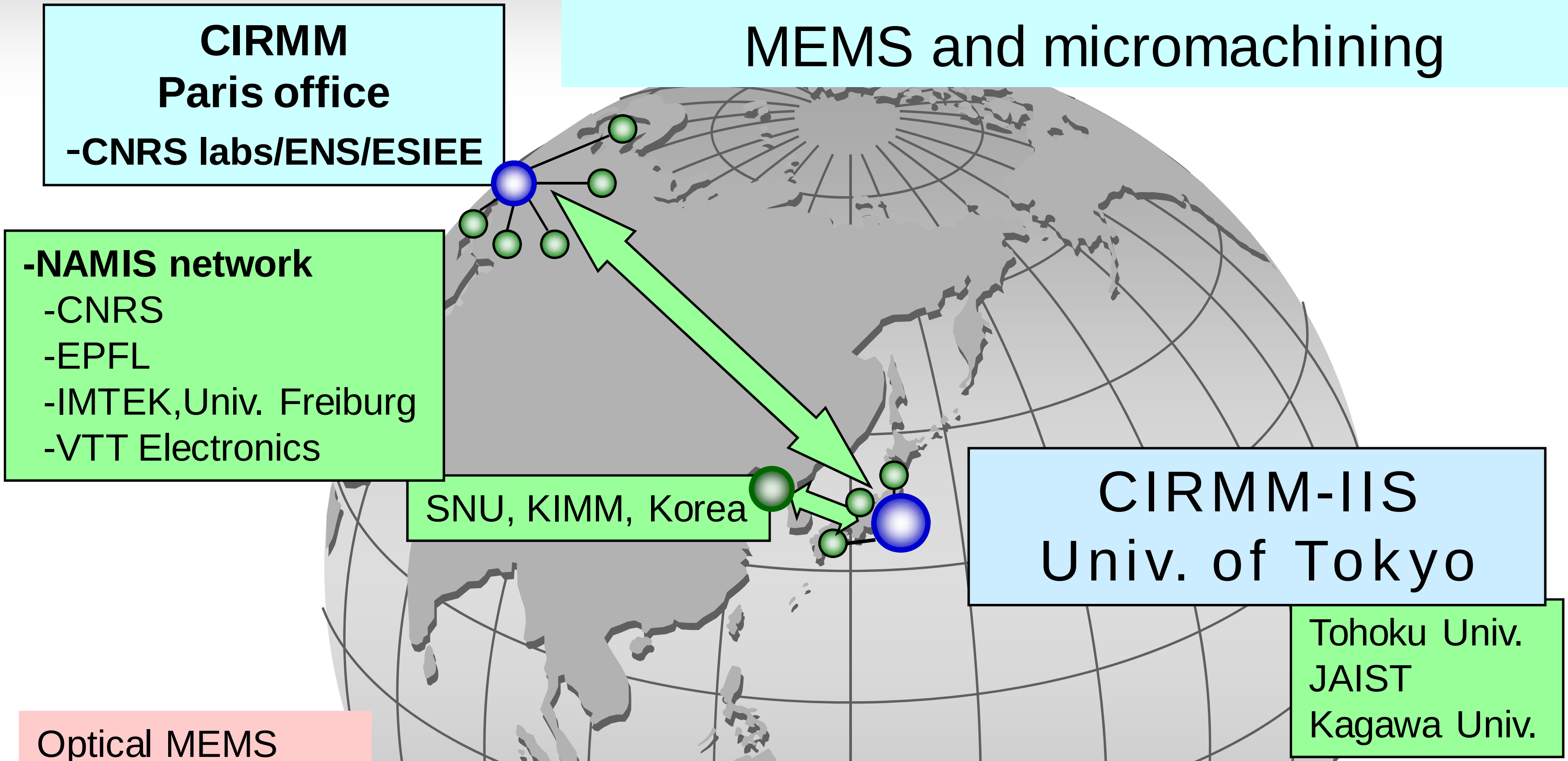
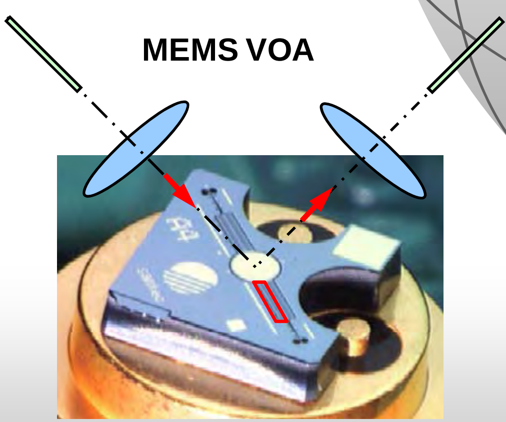
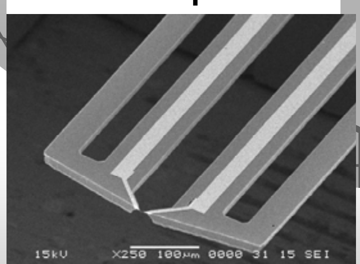
CIRMM for international collaboration on MEMS and micromachining



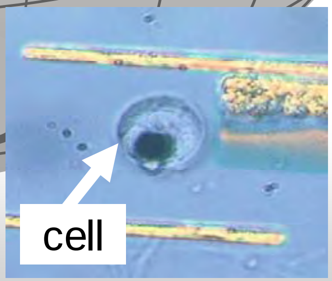
Optical MEMS

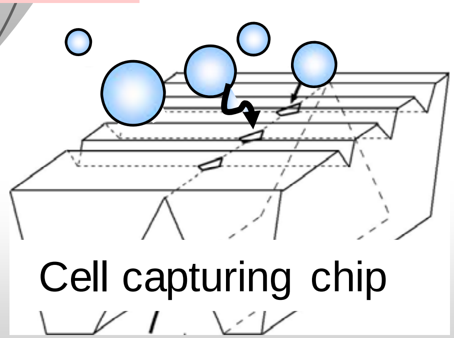


Nano MEMS



Bio-MEMS

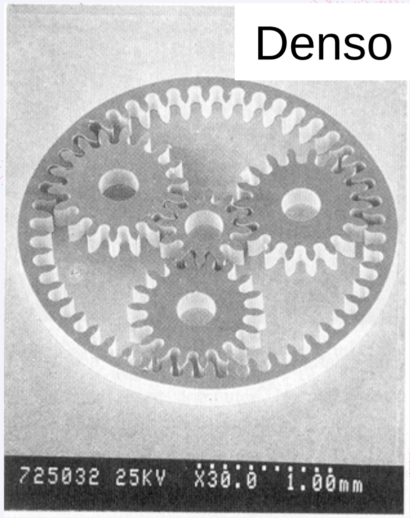




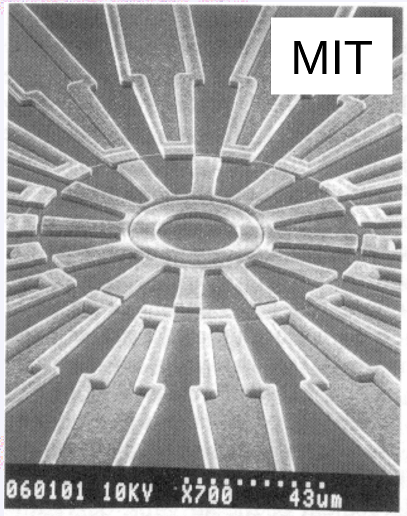
Content of talk

- MEMS
- In-situ TEM observation of nano tensile testing in MEMS
- fL-chamber for confining molecules from diffusion
  - Single molecular analysis of F1-ATPase
  - Microheater for temperature control in ms
- Direct molecular handling
  - Nano-machined tweezers for direct handling of DNA molecule.
  - Molecular sorter driven by Kinesin-MT bio molecular motor.

Various MEMS structures

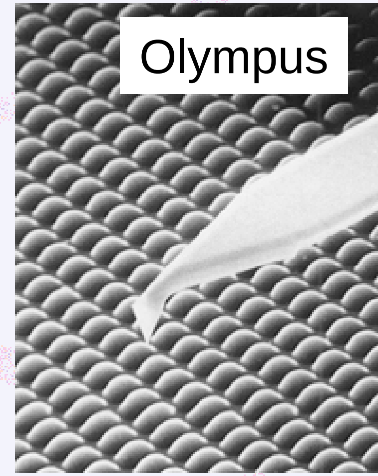


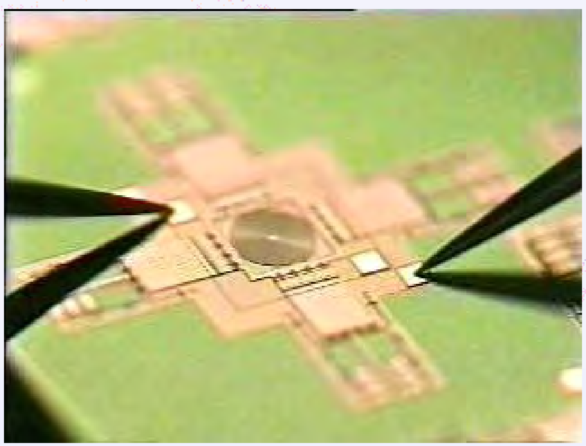
Denso

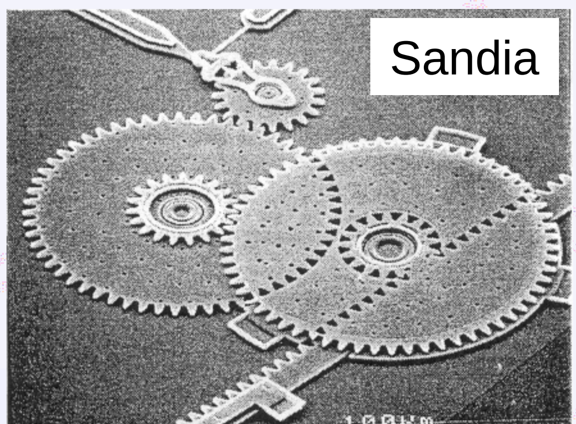


MIT

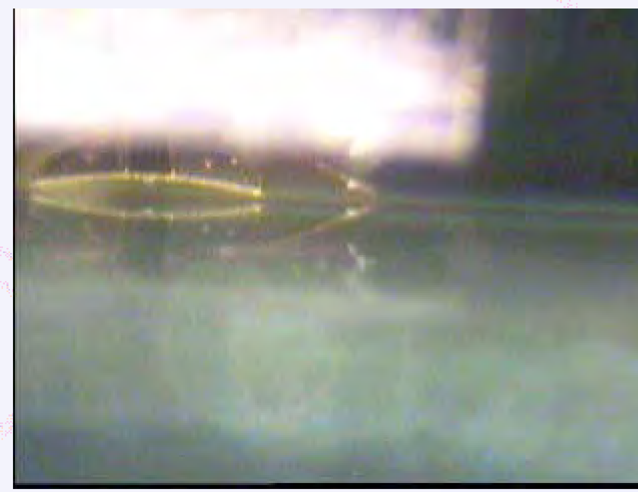
U-Tokyo



Olympus


UC Berkeley



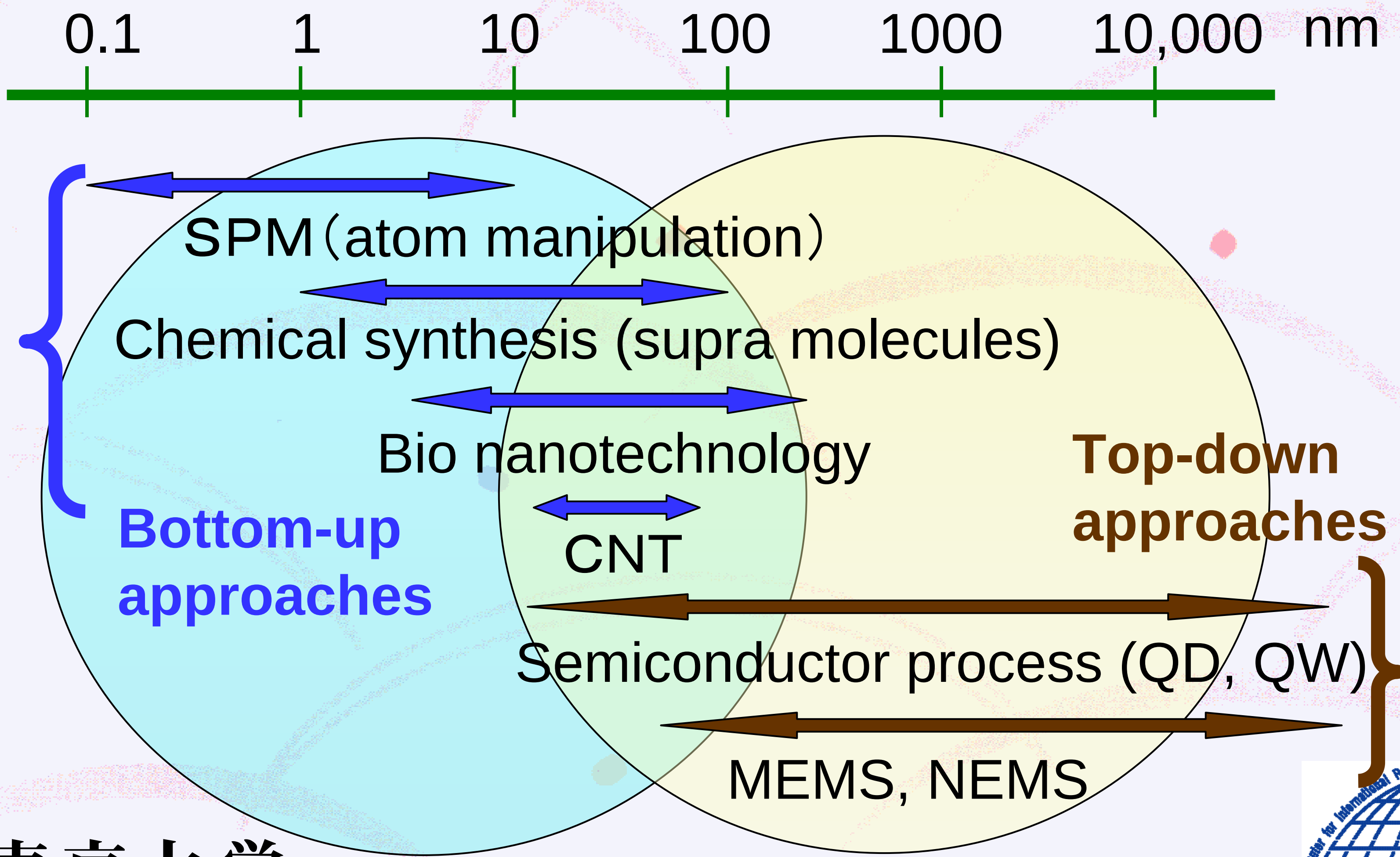
Sandia


Northeastern Univ.

Current MEMS status

- Technologically matured
  - Surface micromachining, D-RIE, CMOS-MEMS, wafer level packaging
- Commercial products are increasing rapidly
  - automobile sensors, projection display, game controller sensors, opto-communication devices, cellular phone devices (resonator, SW, microphone)
- Future directions:
  - nano/bio integration,
  - large-area MEMS

Bridging nano and micro worlds by combining bottom-up & top-down technology



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In-situ TEM observation of tensile testing of Si nano wire

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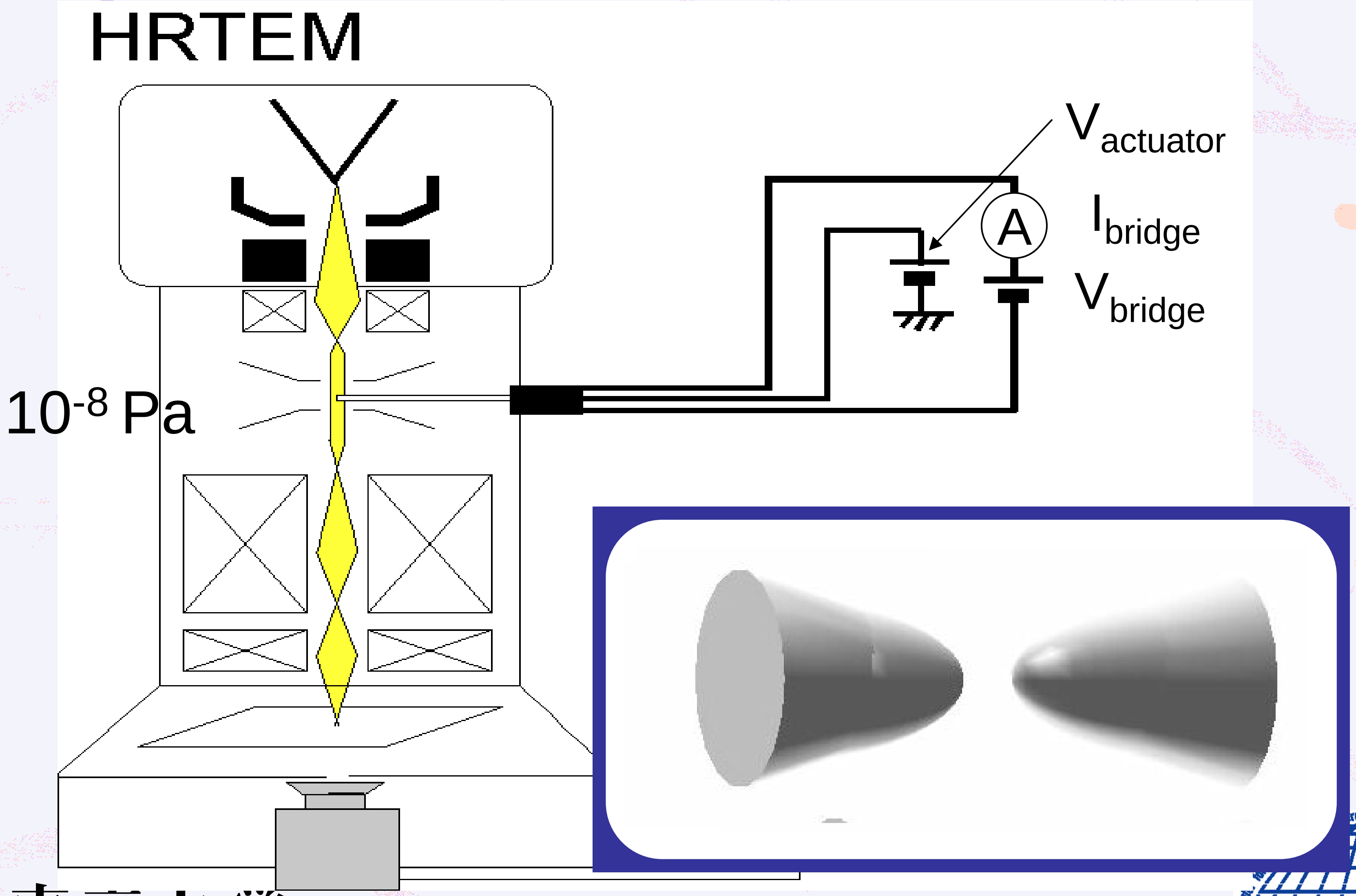
Simultaneous TEM observation and current measurement during tensile testing



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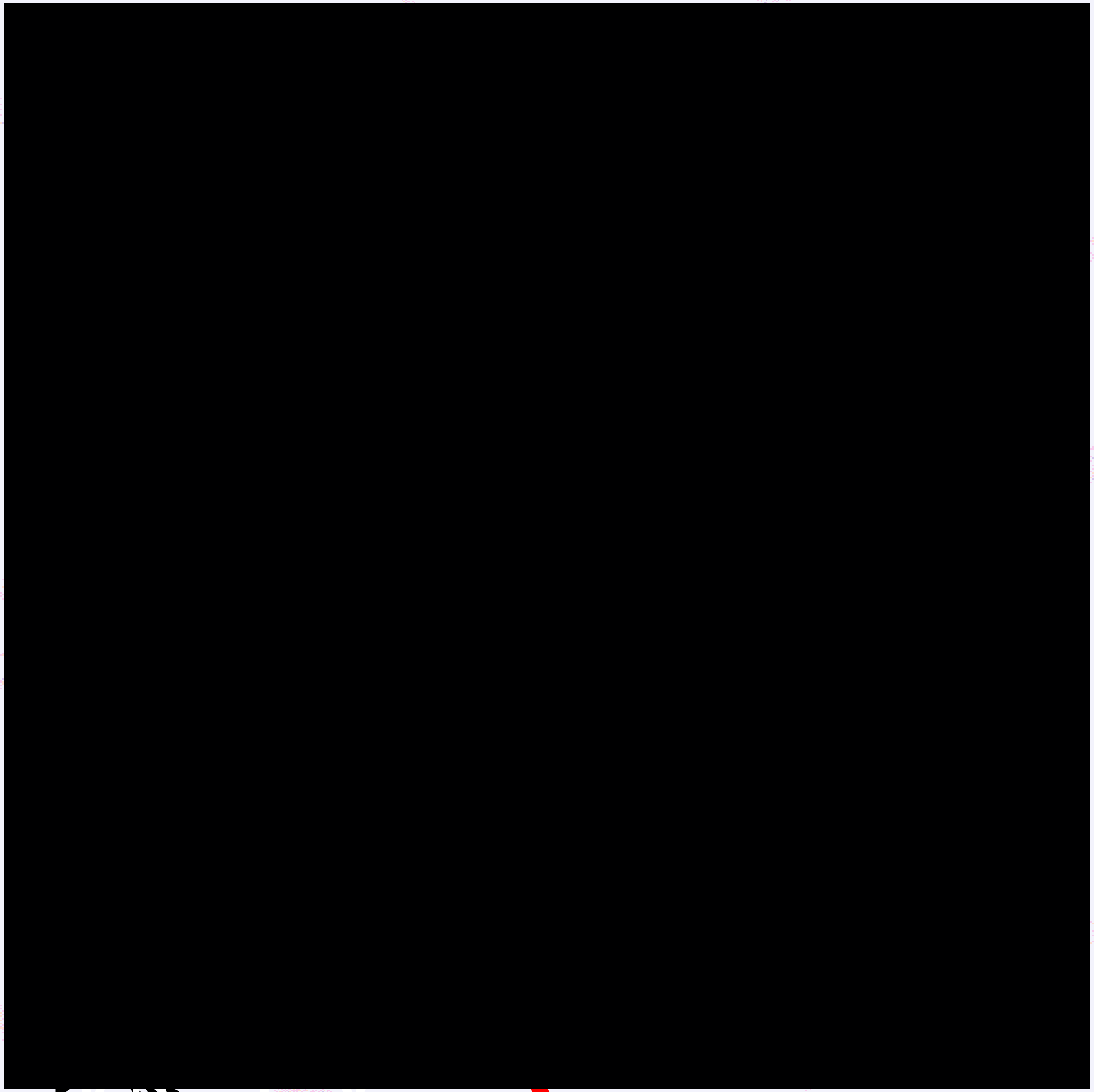
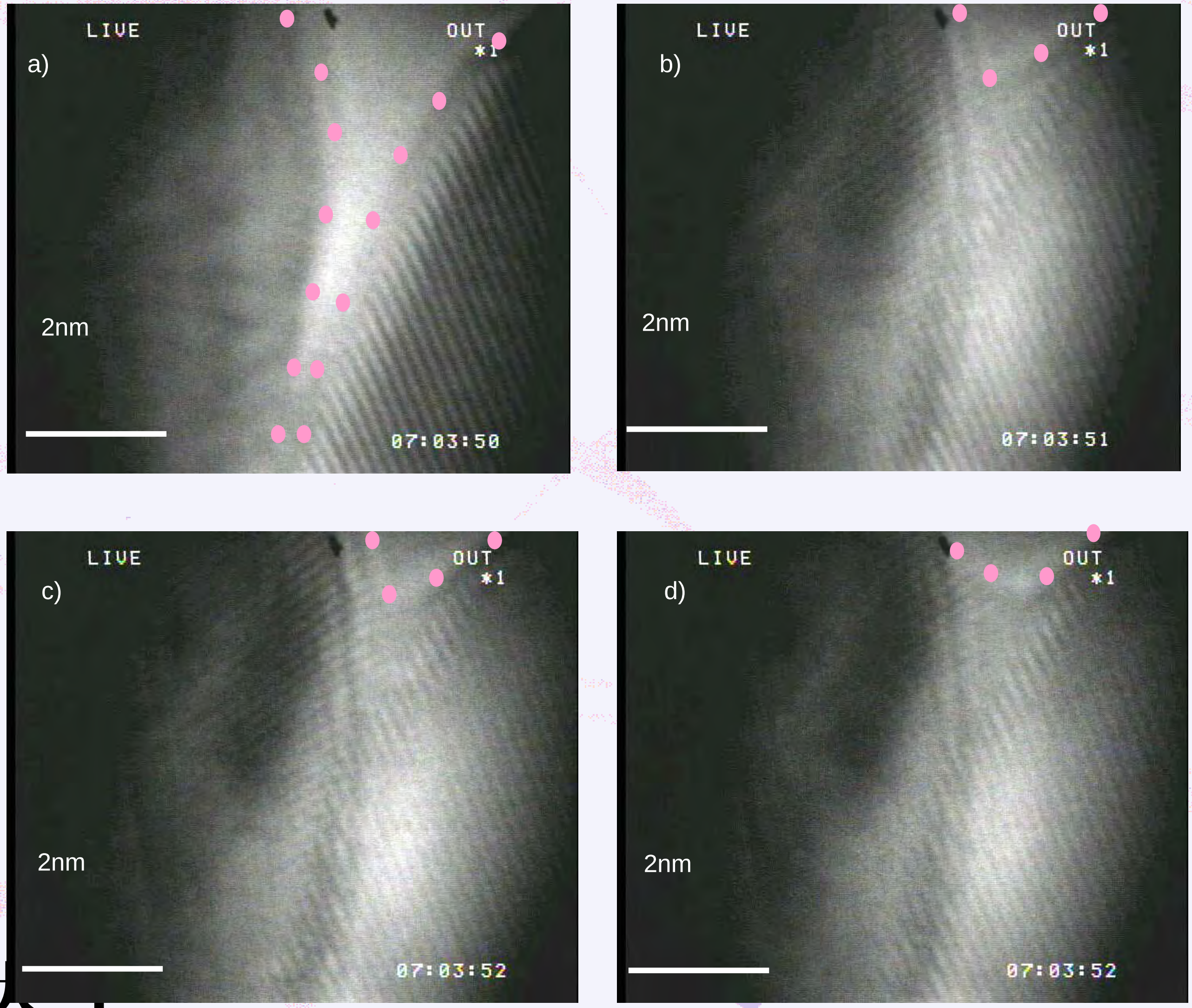
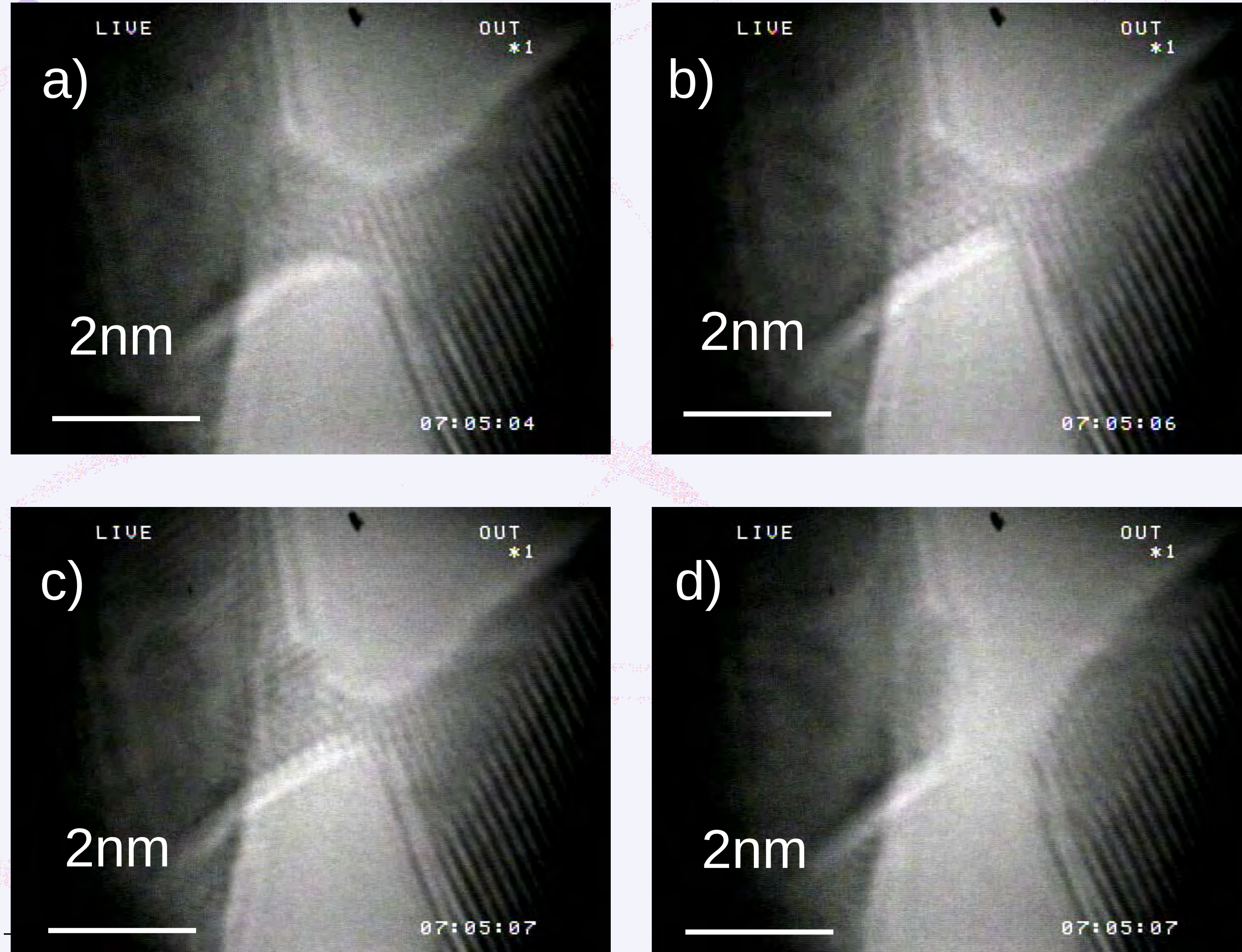
In-site TEM observation of tensile testing of nano wire



Au-Au nano contact formation



Au-Au nano contact breakage



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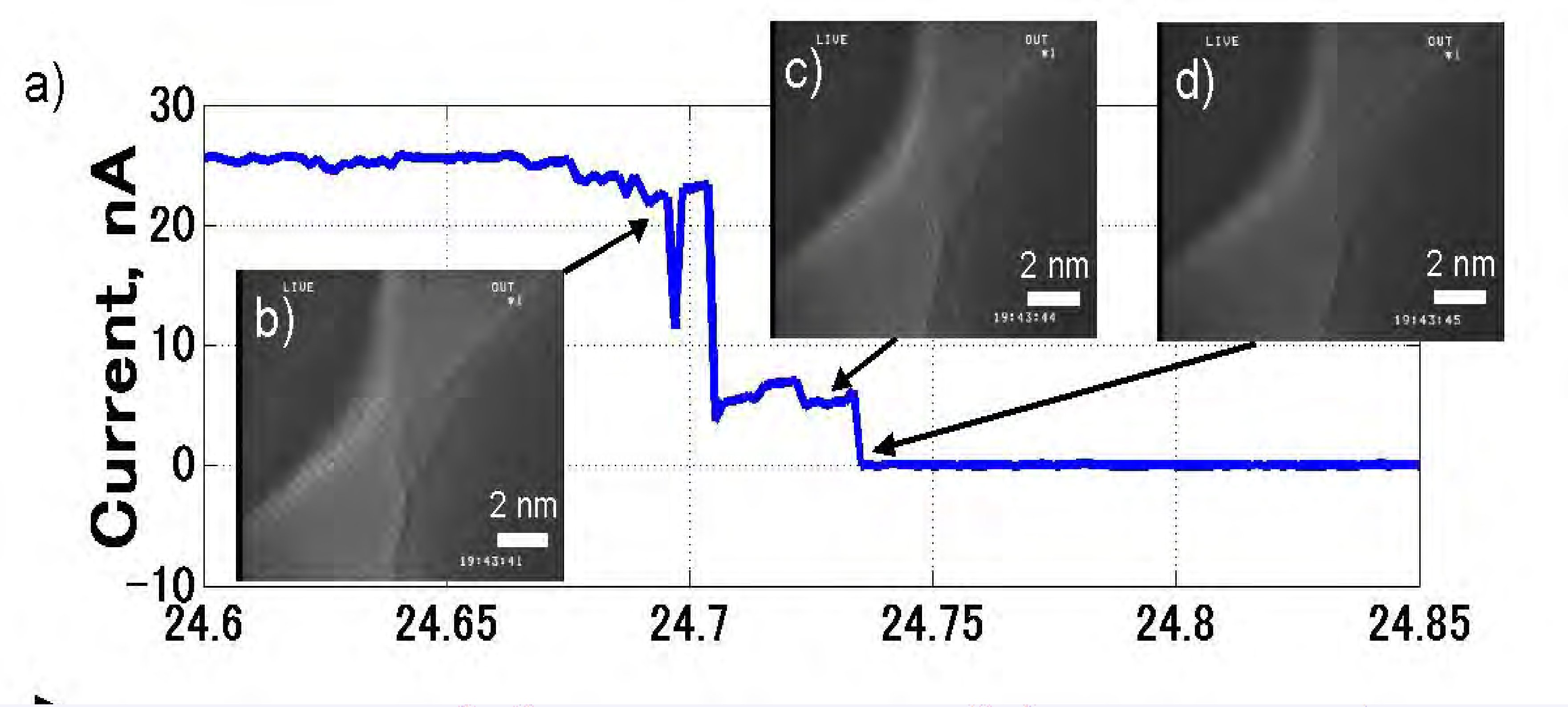
Current vs contact shape



Actuation voltage was maintained at 125.3 V. The restoring force of the tip support broke the gold contact.

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DNA handling by MEMS tweezers

M. Kumemura, H. Sakaki, C. Yamahata,
D. Collard, H. Fujita

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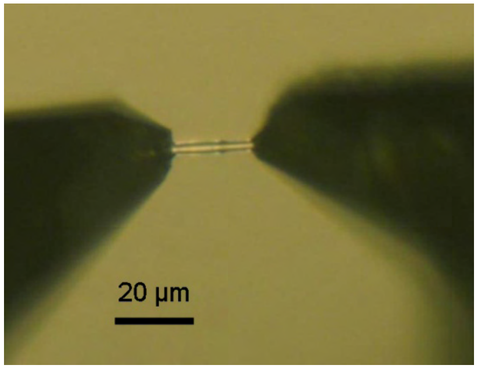
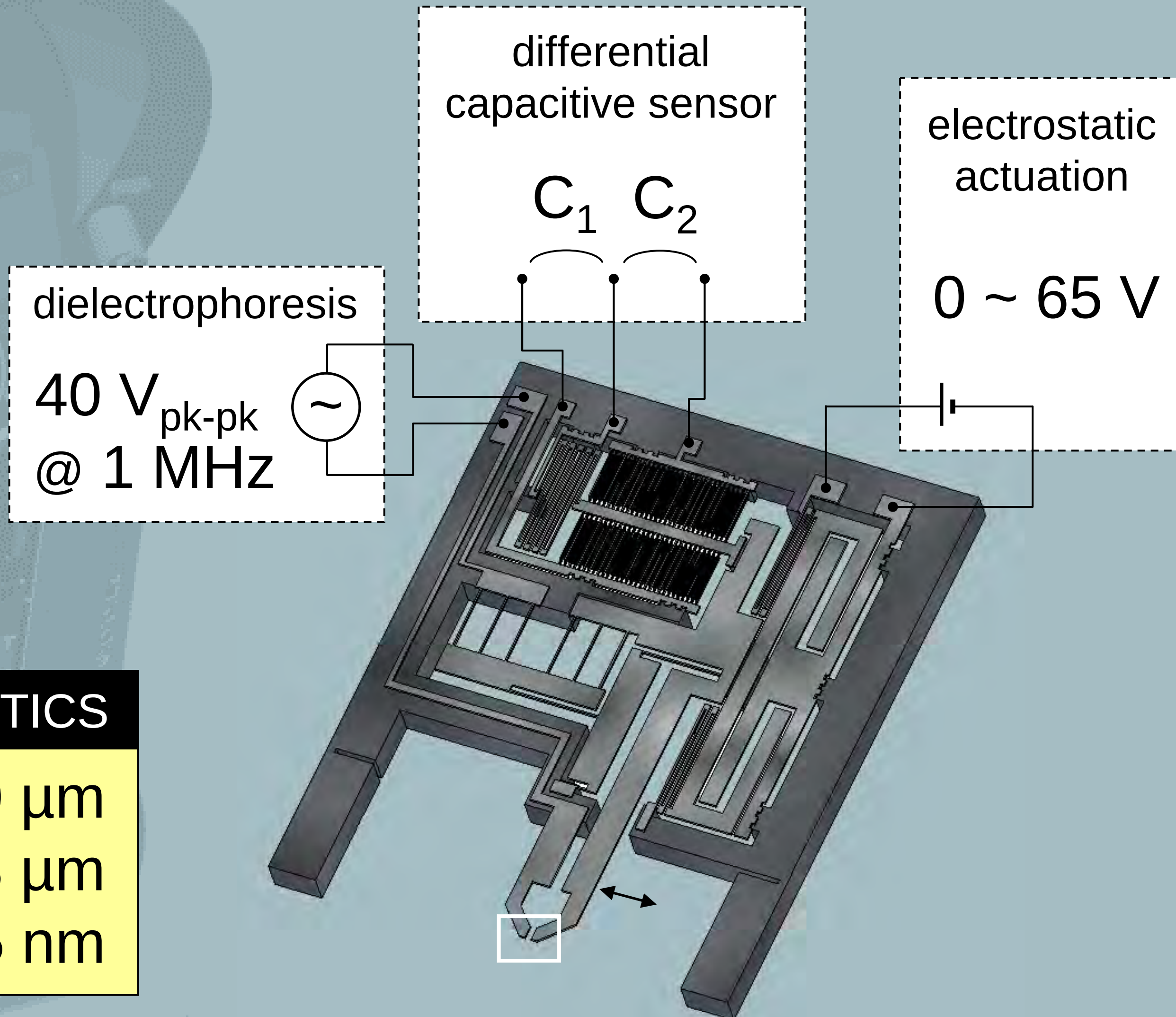
Mechanical & Electrical characterization of DNA bundles

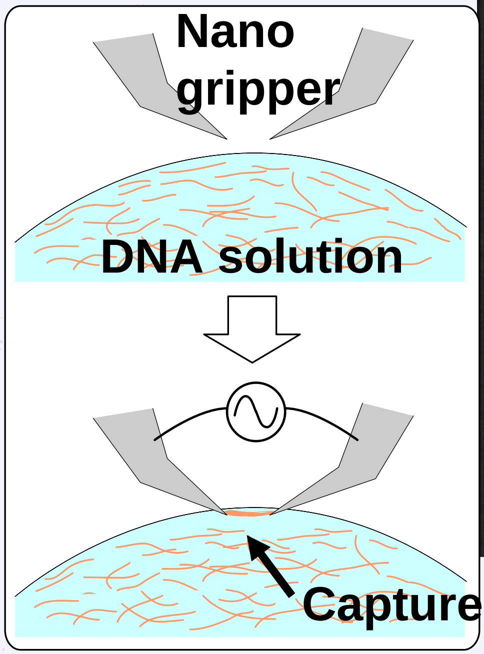
Bundle of DNA

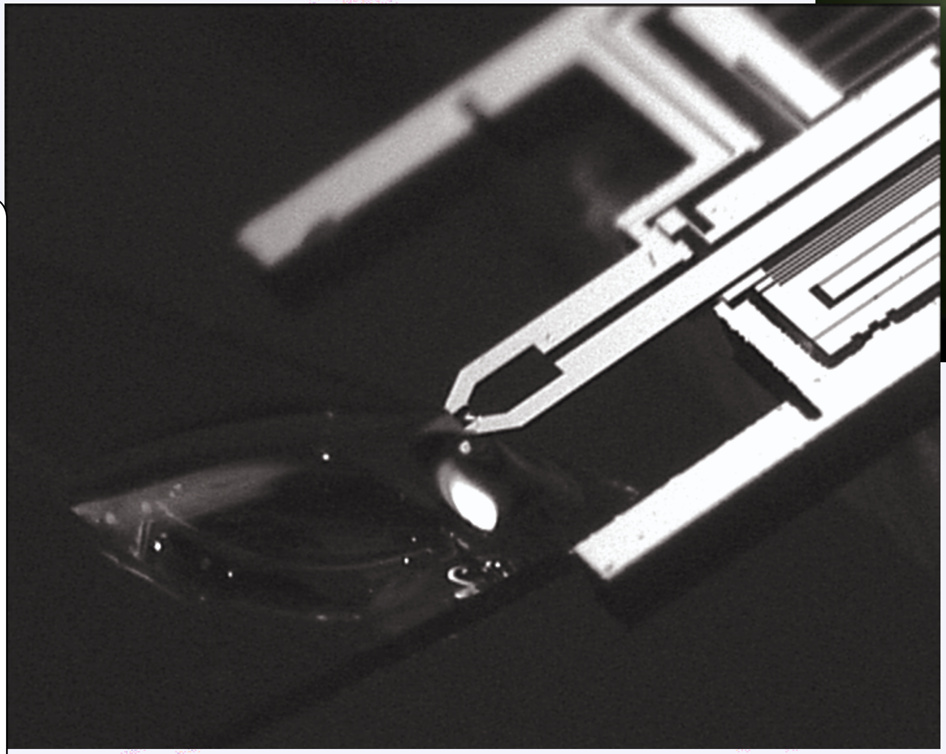


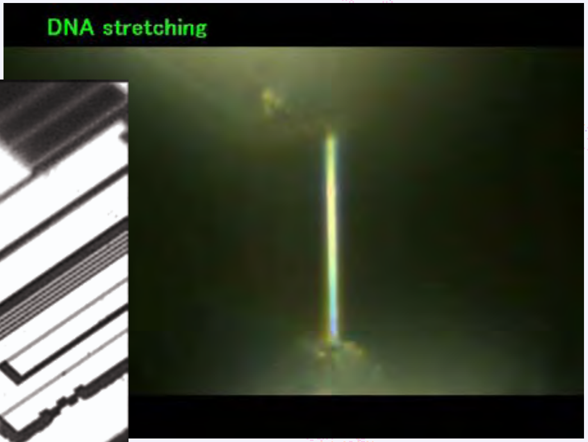


MAIN CHARACTERISTICS	
Initial gap:	20 µm
Displacement range:	3 µm
Resolution:	5 nm

Tweezers approaching droplet containing DNA to capture them







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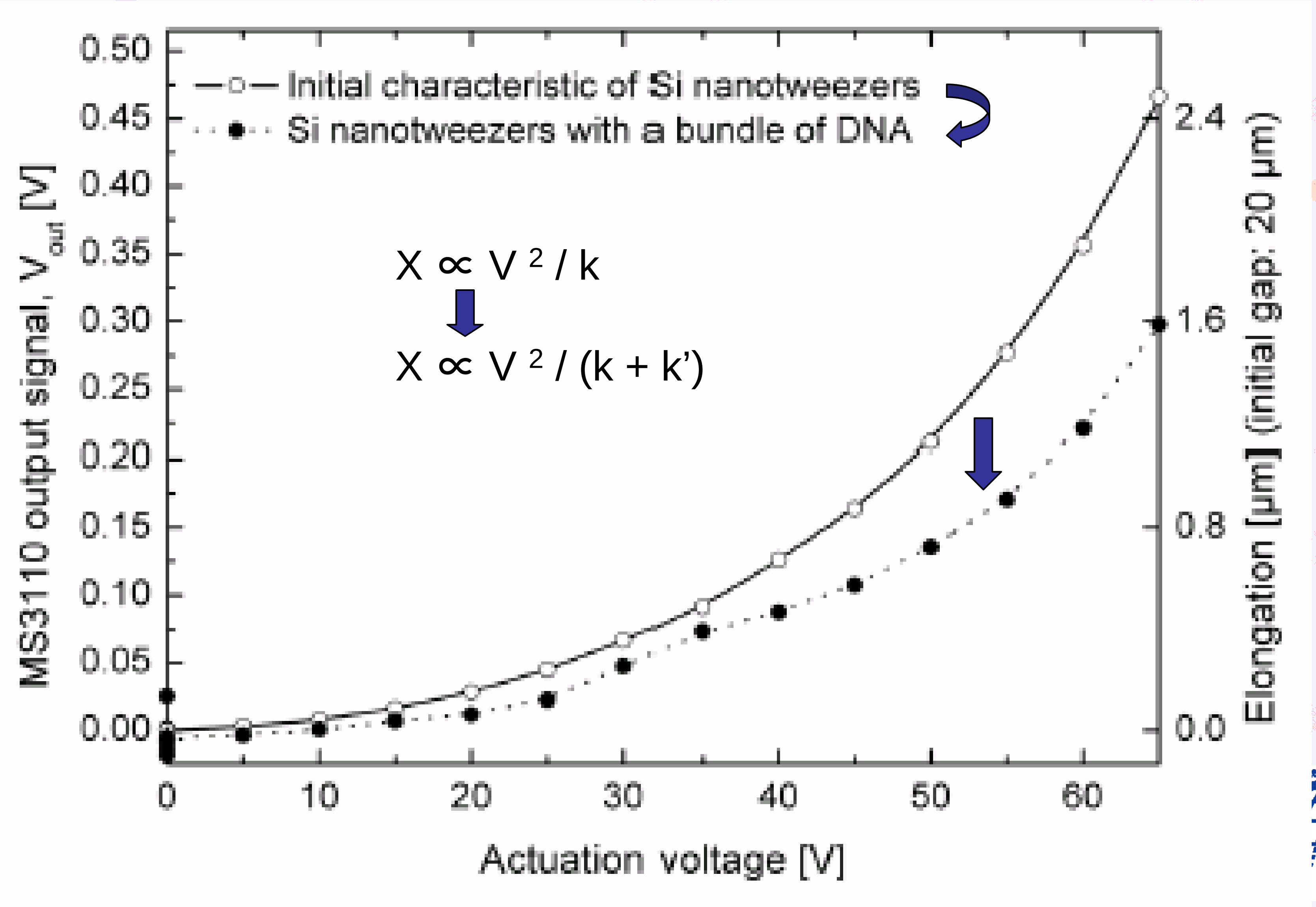
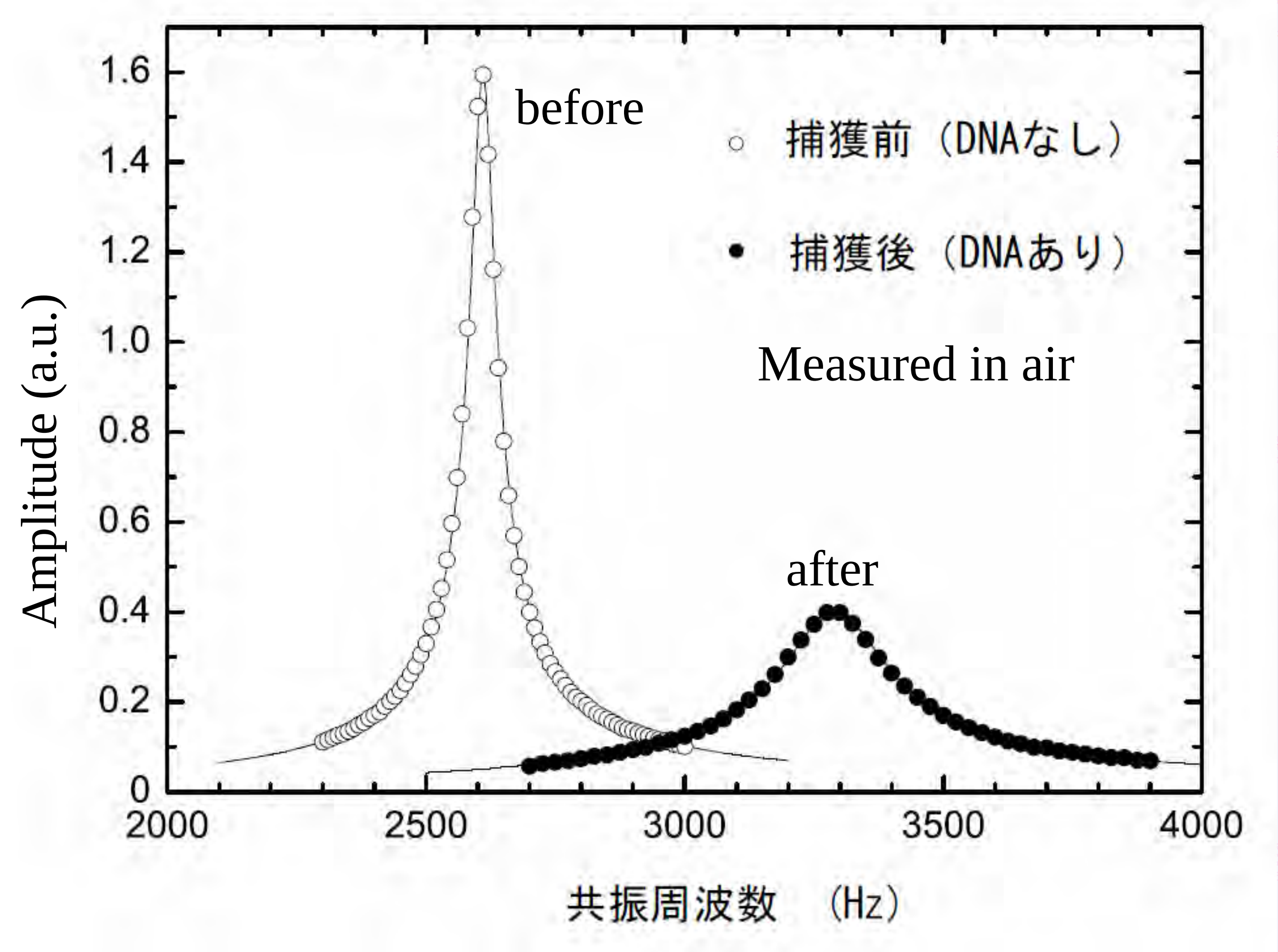
Mechanical characterization



◎Mechanical characterization of DNA bundles

Resonant characteristics before/after capturing DNA



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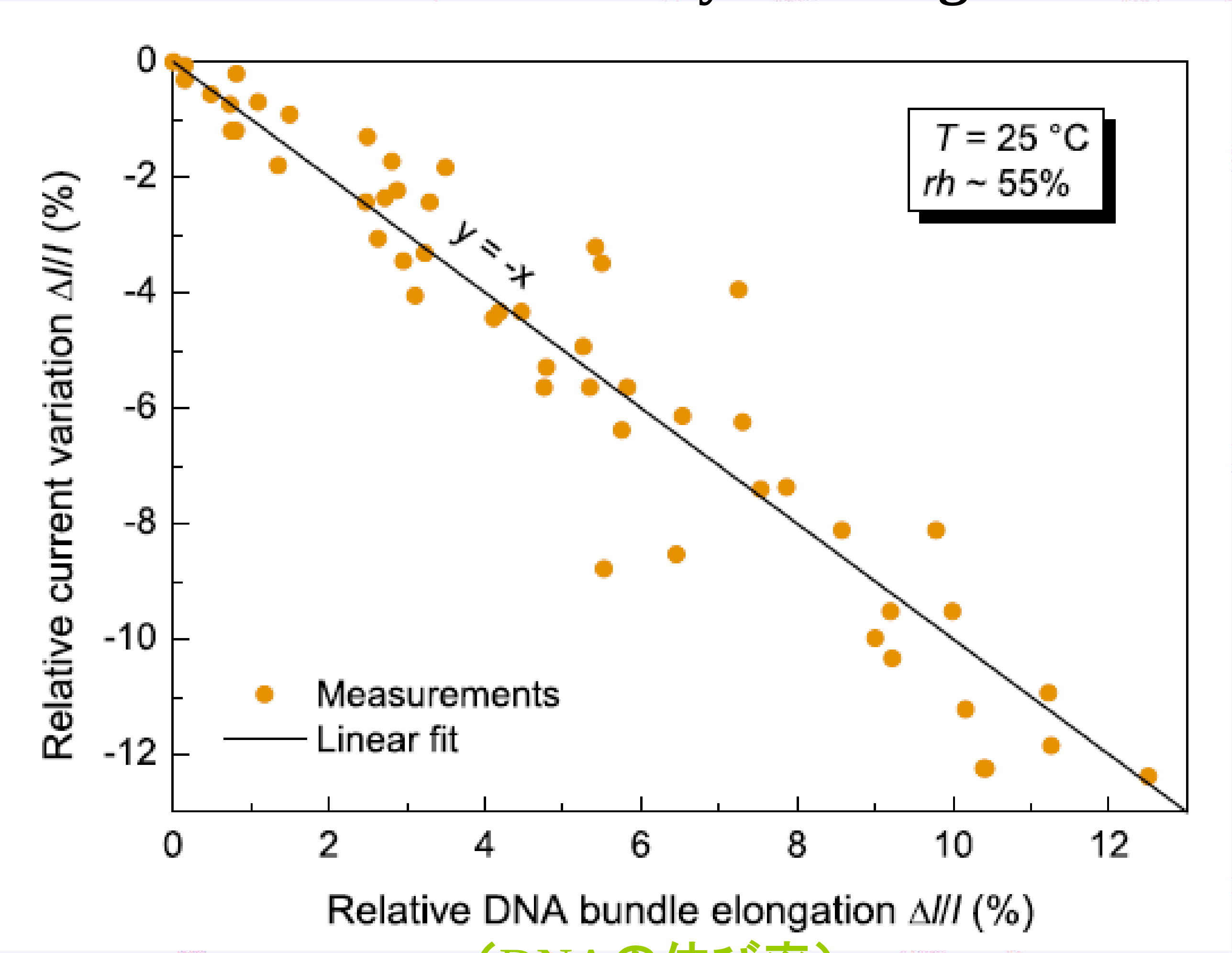
◎Electrical characterization of DNA bundles

Measurement of conductivity vs. elongation

（電流値の変化量）



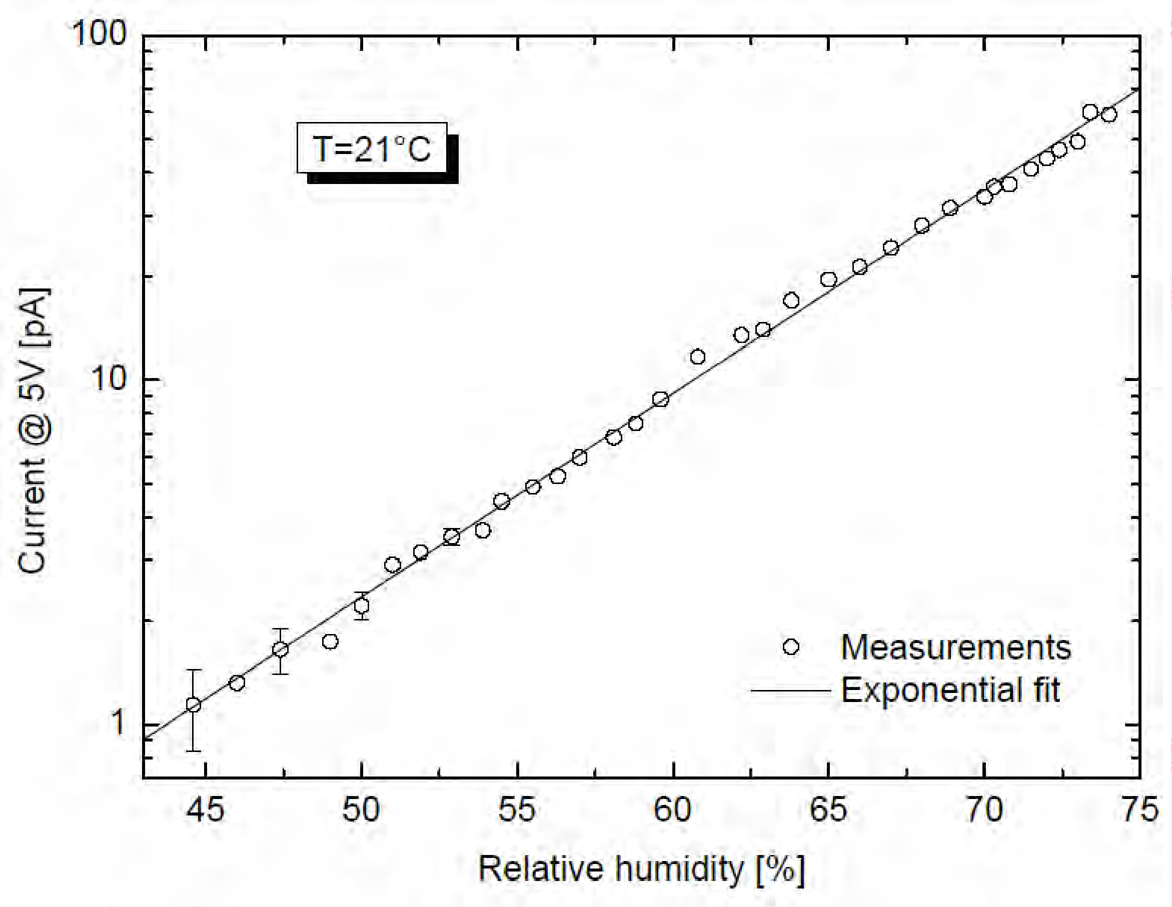
（DNAの伸び率）

Linear decrease of conductivity

$$R = \phi * \frac{L}{S}$$

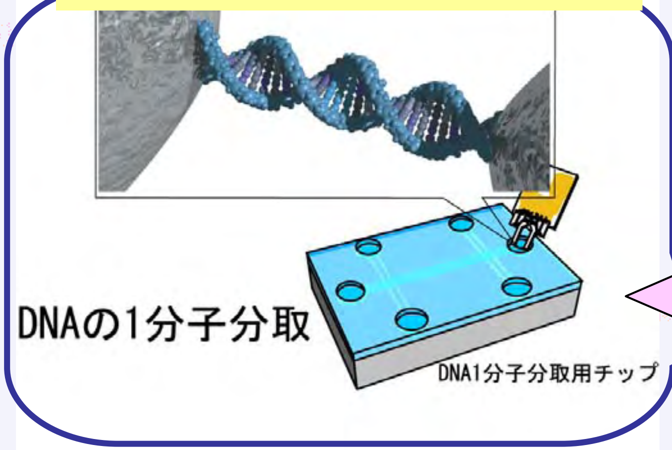
Current flow through a DNA bundle

Exponential decrease of the current with decreasing humidity.
Data extracted from previous measurements (**5V step**) after **60 sec.**
(rh was decreased from 75% to 45% in 6 hours)

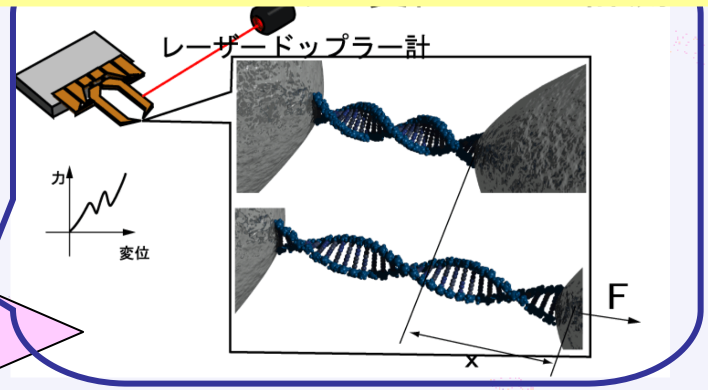


Prospected single molecular characterization of DNA by nano tweezers

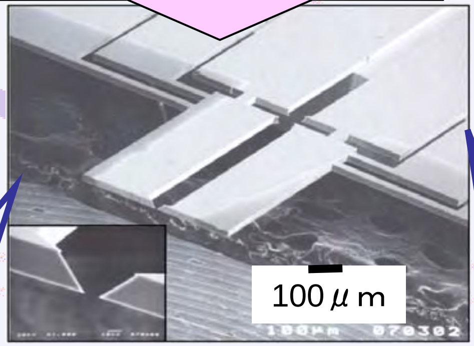
Separation and retrieval of a single DNA molecule



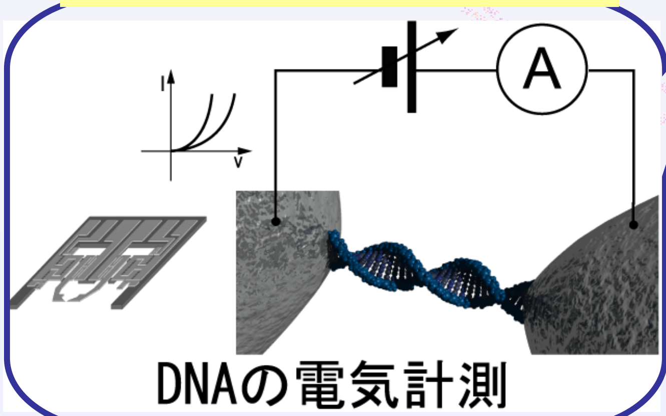
Stress vs. strain measurement



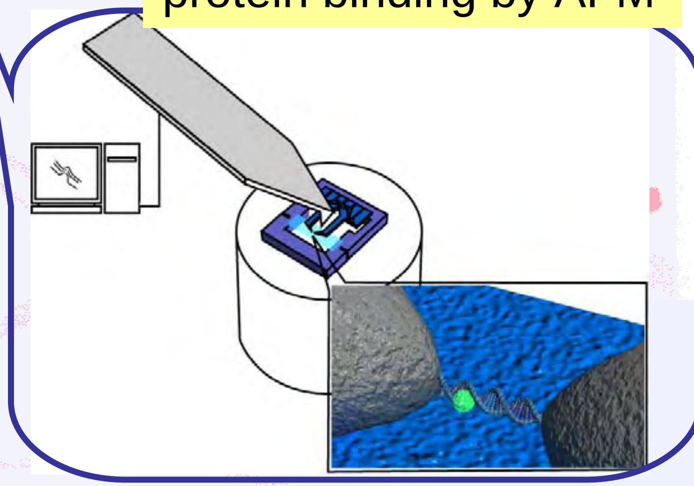
DNA tweezers



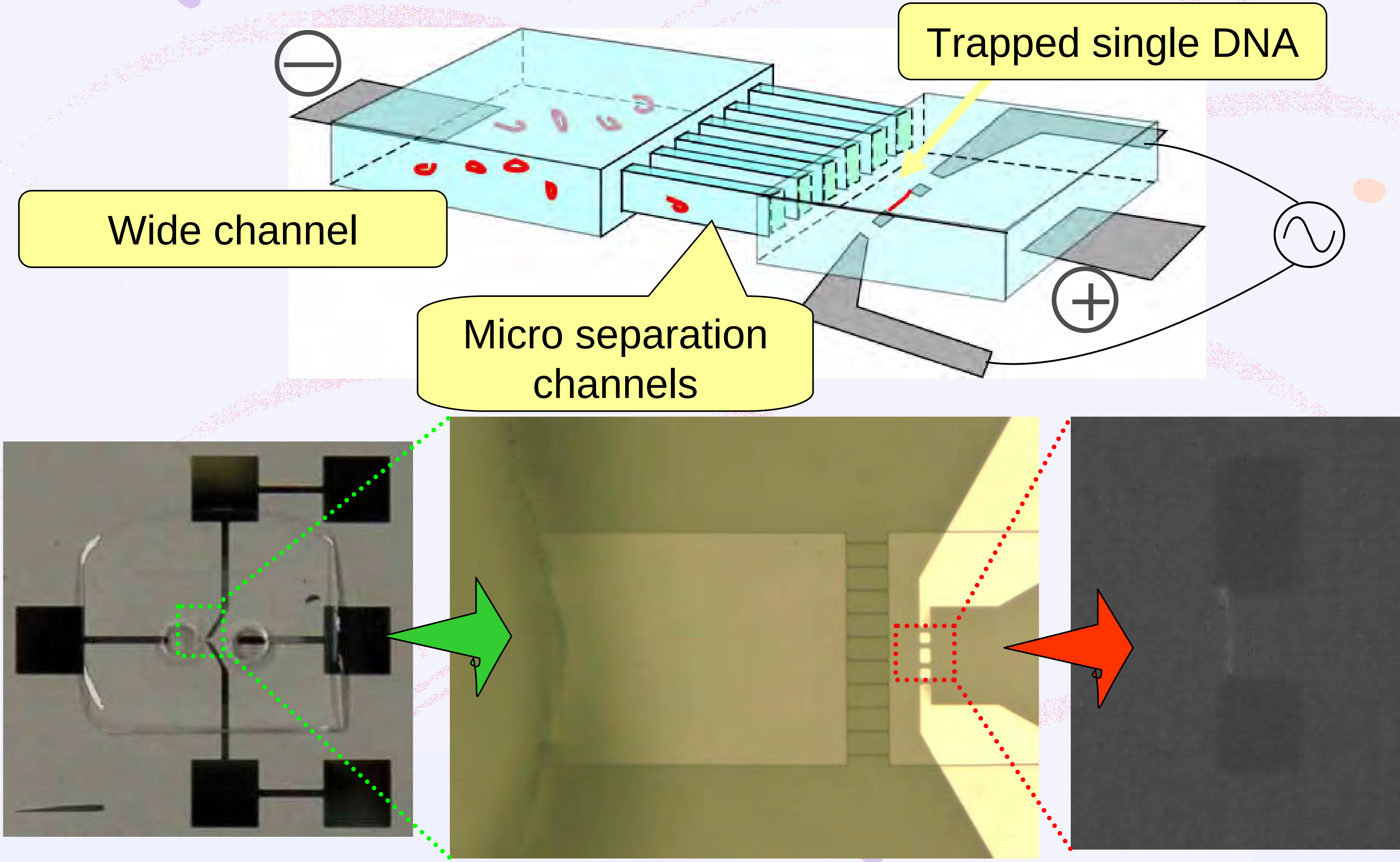
Electrical measurement



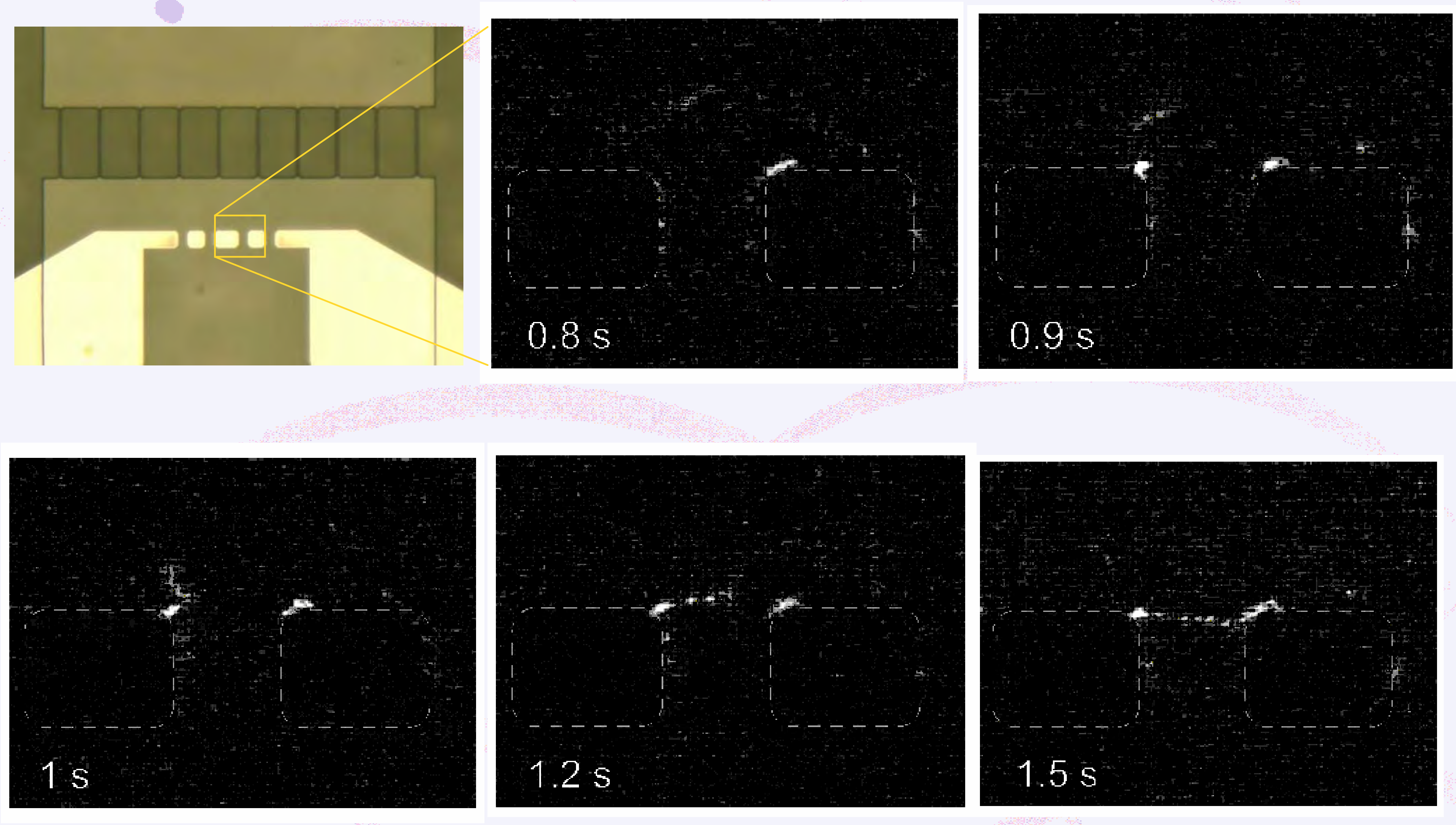
Visualization of DNA protein binding by AFM



Single molecular separation and trapping



Single molecular trapping sequence



M/ Kumemura, et al. ChemPhysChem (2007)

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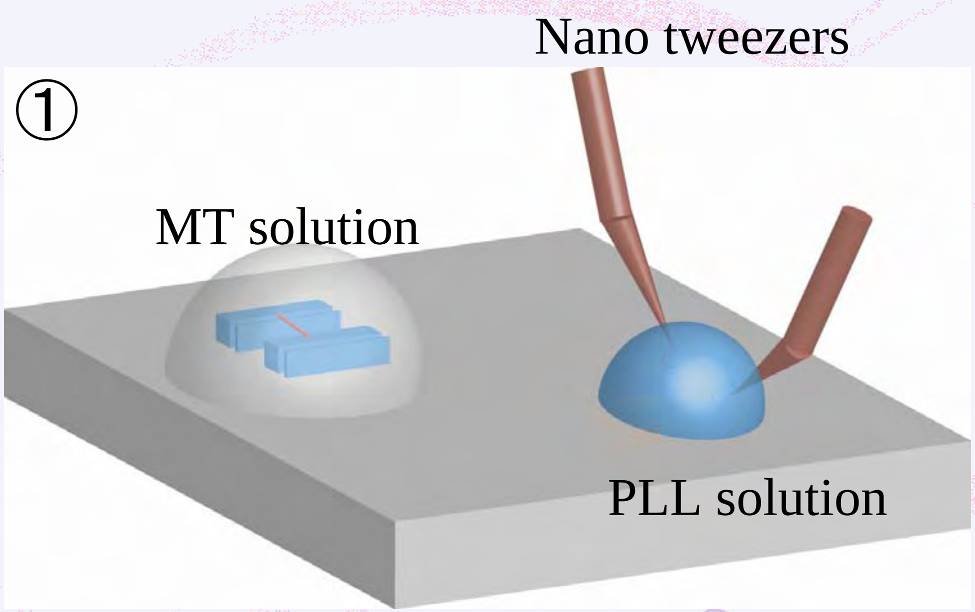
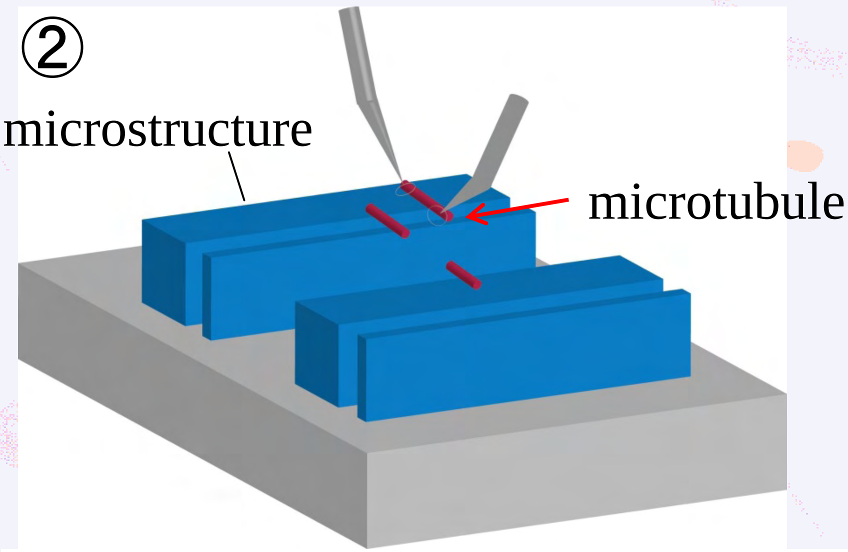
Capturing a single microtubule



Coating tweezers tips with PLL



A single MT bridging over a gap was captured by tweezers

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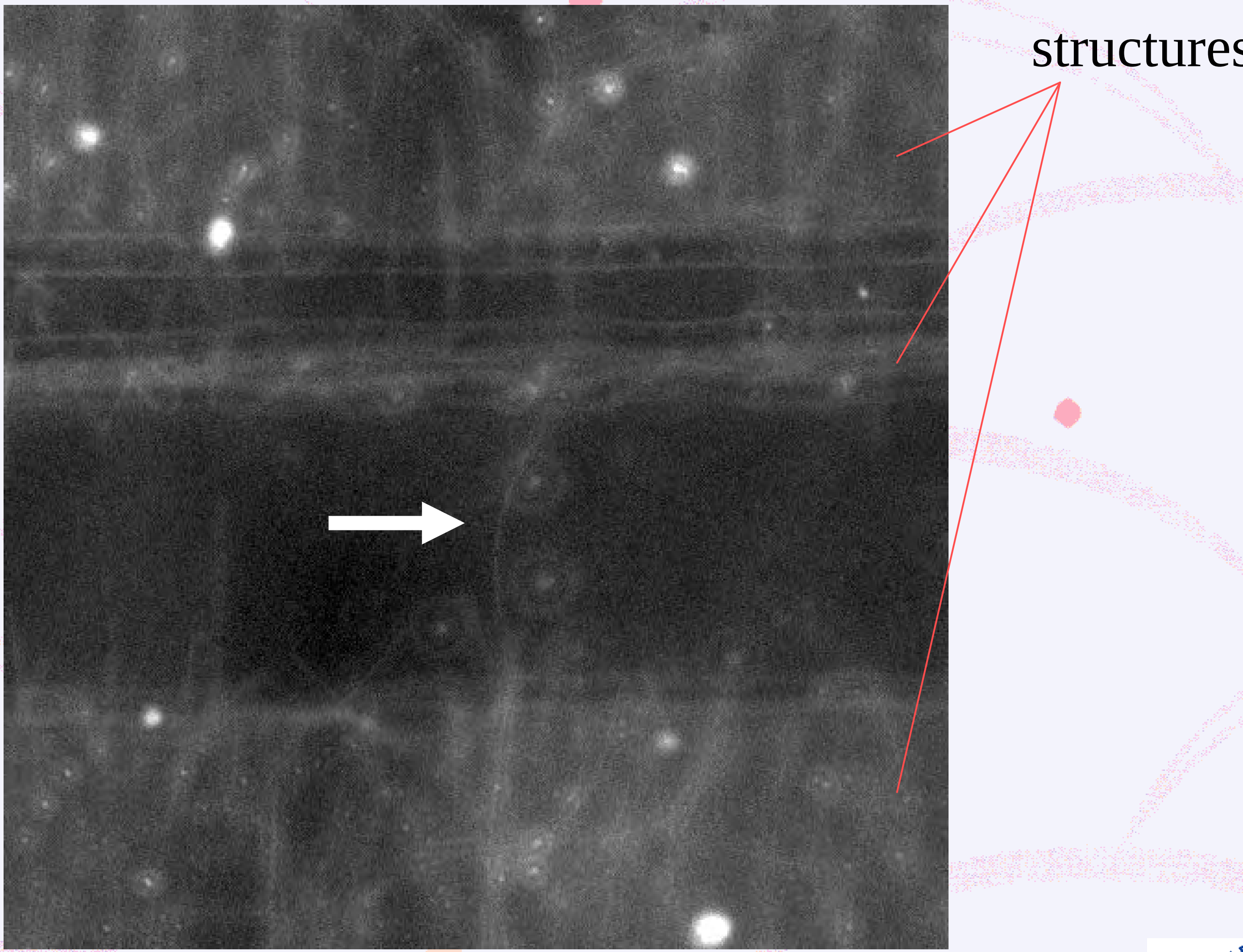
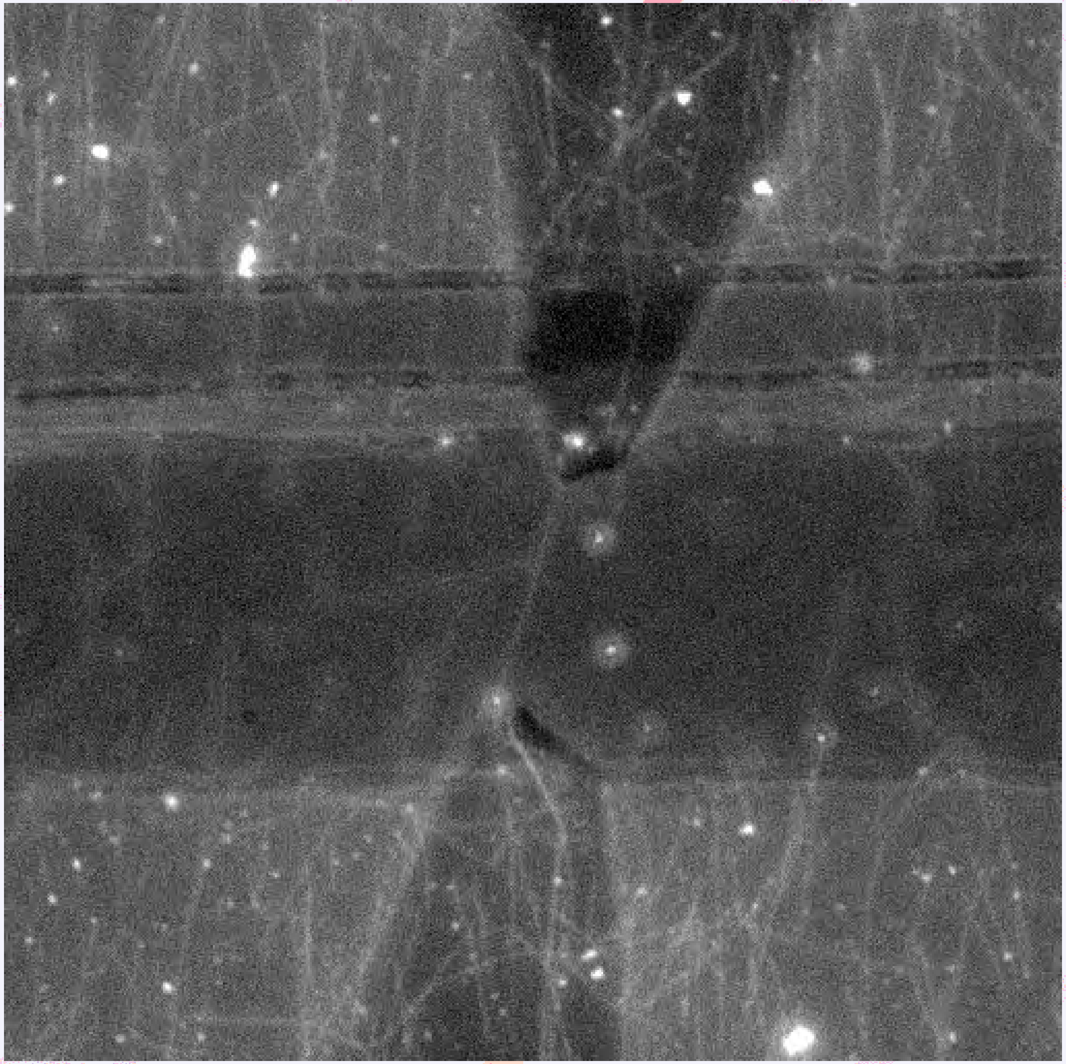
Capturing a single microtubule



Capturing a single microtubule



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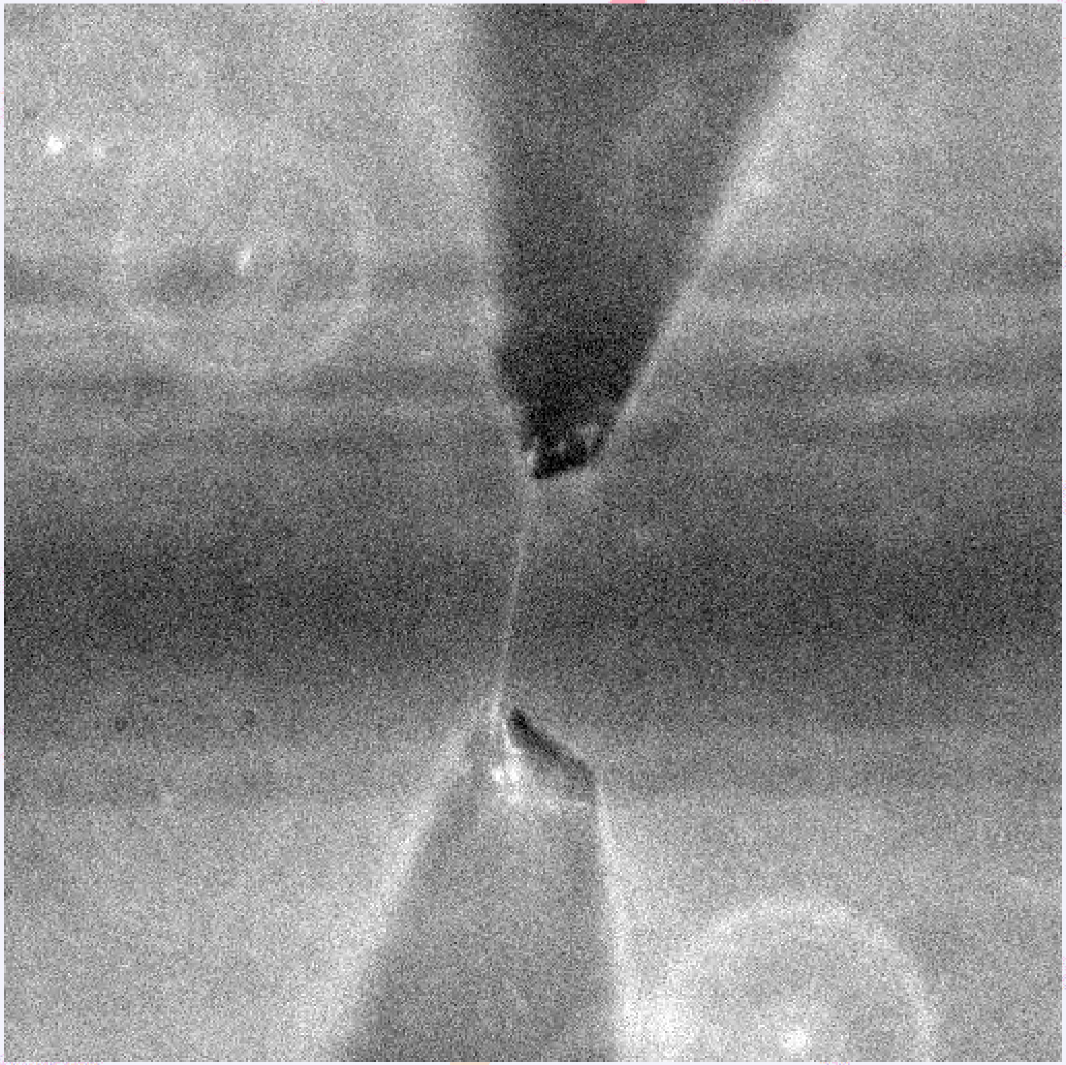
Capturing a single microtubule



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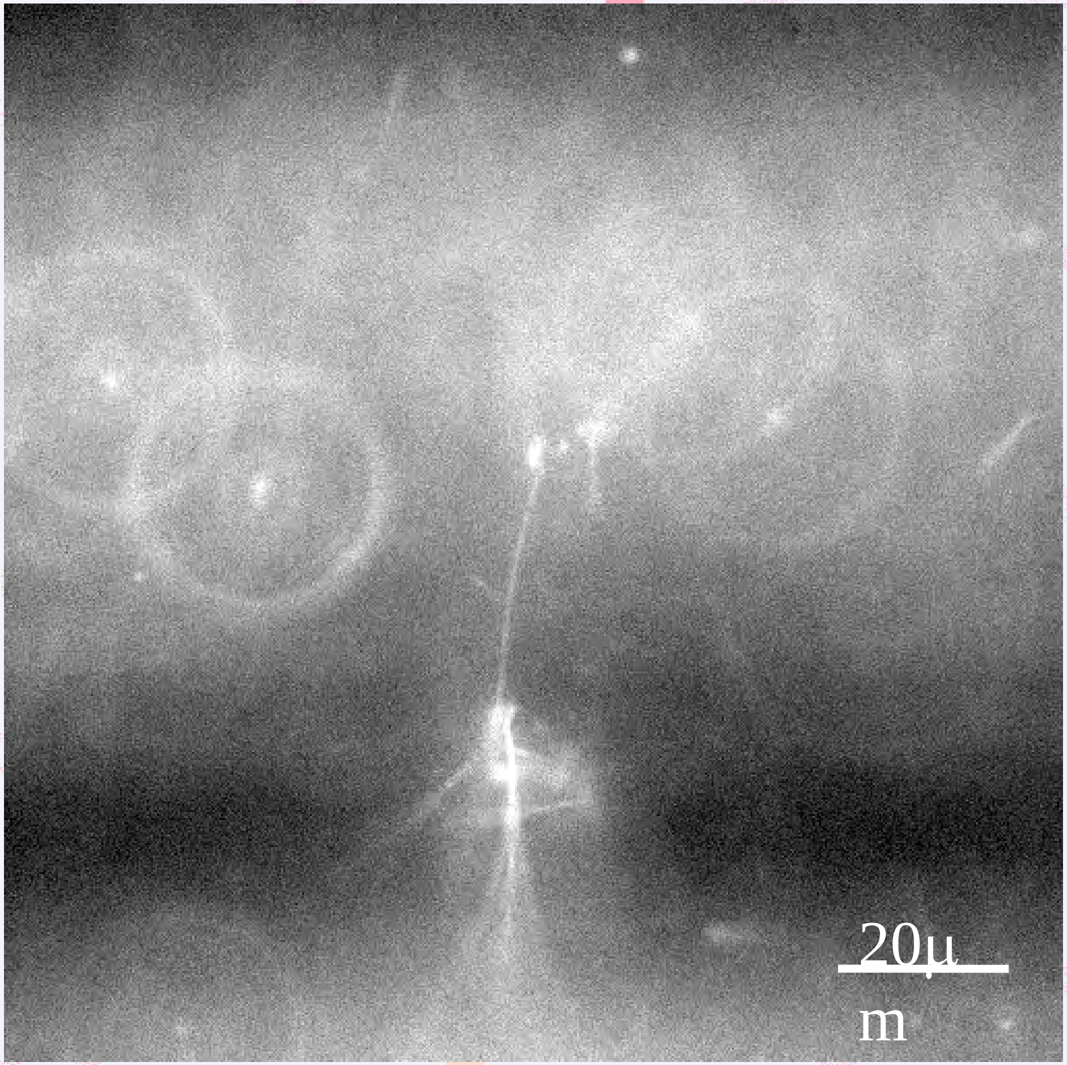
Captured single microtubule by florescent image



The microtubule can be placed on PLL coated glass substrate.

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Visualization of Bio Motor Molecule and Single Molecular Characterization of its Chemical Activity

in collaboration with
Prof. Hiroyuki Noji (Osaka-U),
Prof. Shoji Takeuchi (IIS/U-Tokyo) &
Dr. Yannick Rondelez* (LIMMS/CNRS-IIS)

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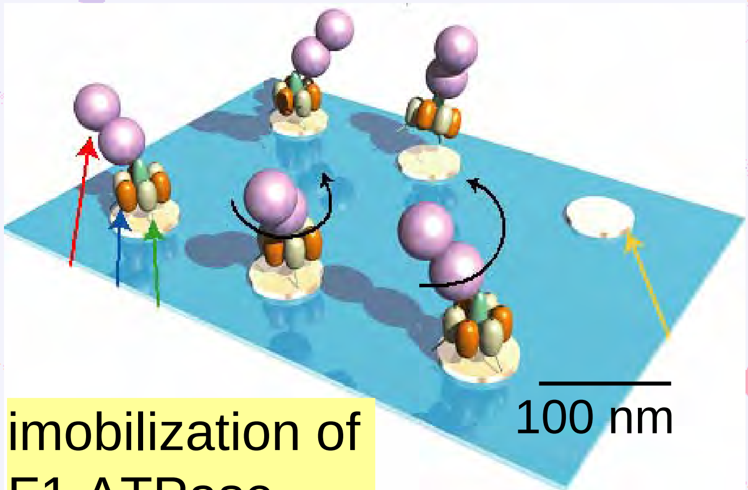
Single molecule/cell analysis

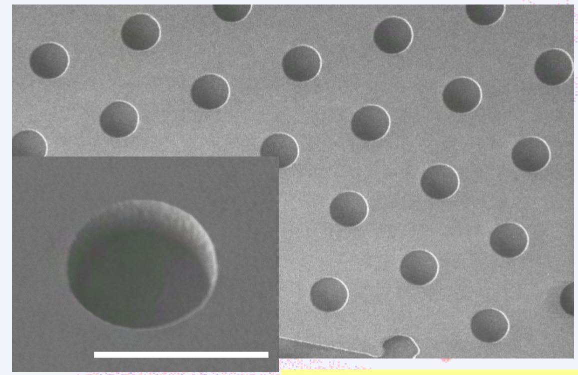
- Advantages:
  - Time course measurement
  - Distribution analysis (average + dispersion)
  - Fast screening
  - Individual correlation between parameters
- Challenging requirements:
  - Extreme high sensitivity
  - Many measurement points
  - Very fast measurement and control equipments
  - Visualization
- MEMS can solve most problems.
  - High sensitivity, parallel processing, high speed, imaging in liquid

F1 ATPase in fL chamber

in collaboration with Prof. H. Noji & S. Takeuchi

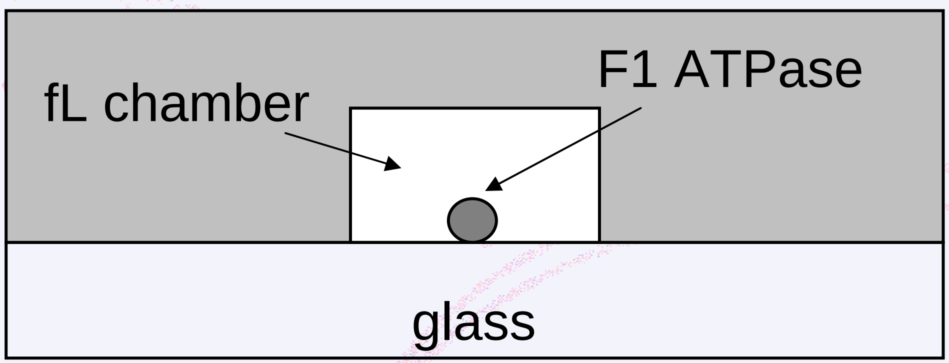


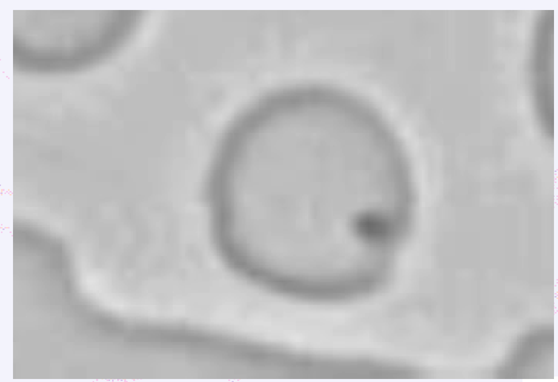
imobilization of
F1 ATPase



6 μm

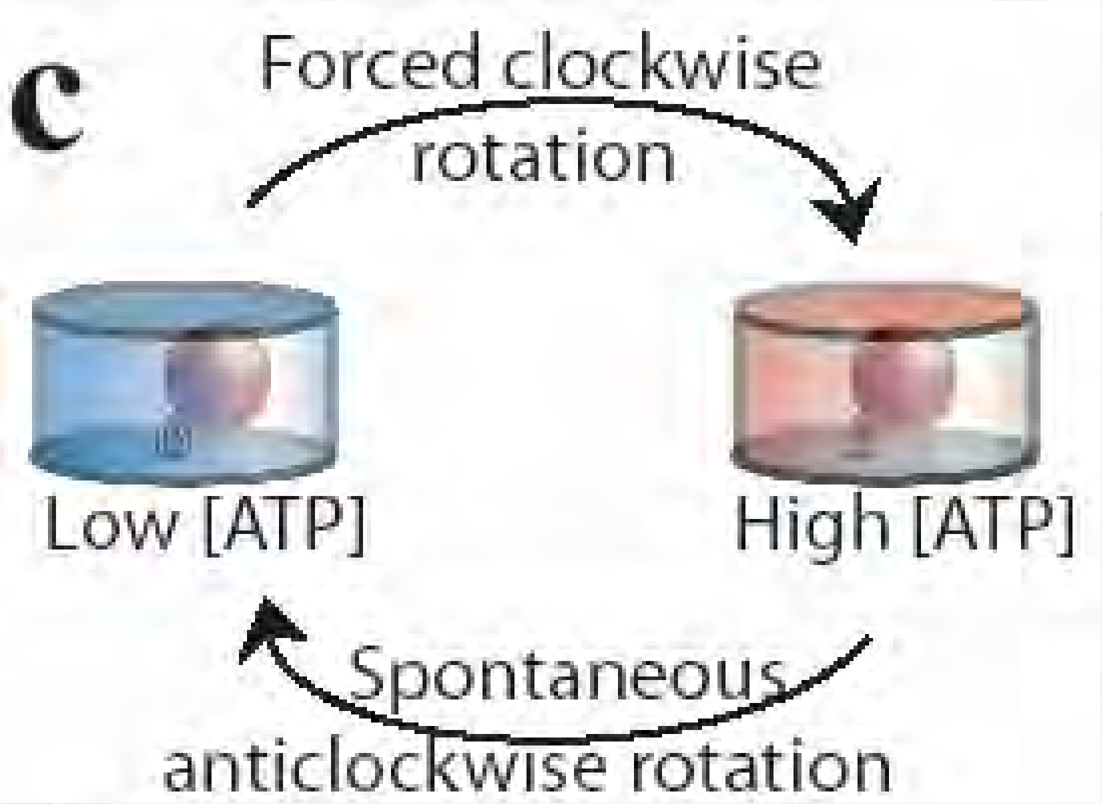
PDMS fL chambers



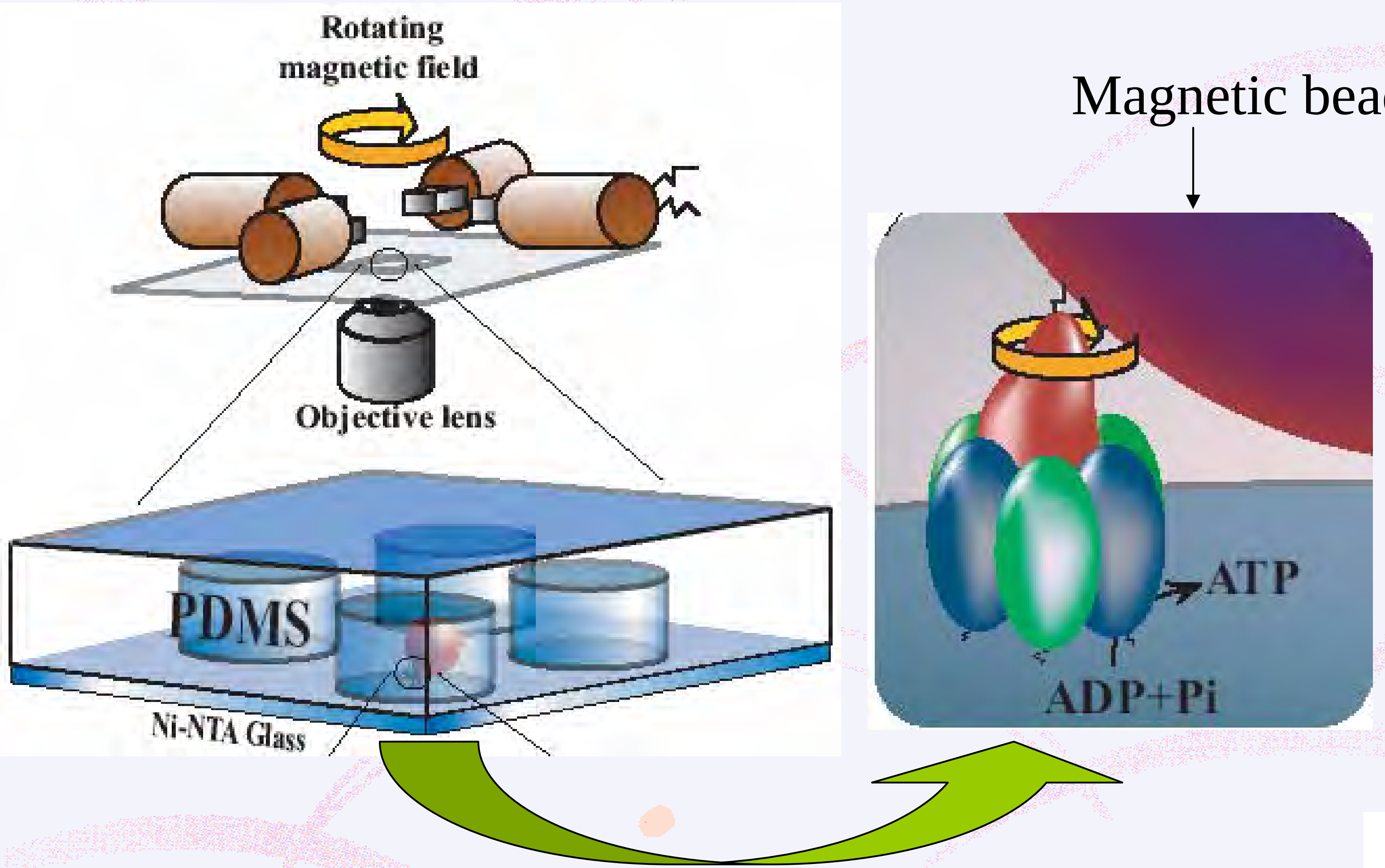


5 μm

ATP synthesis by mechanical rotation of F1-ATPase



Magnetic force drove F1-motor



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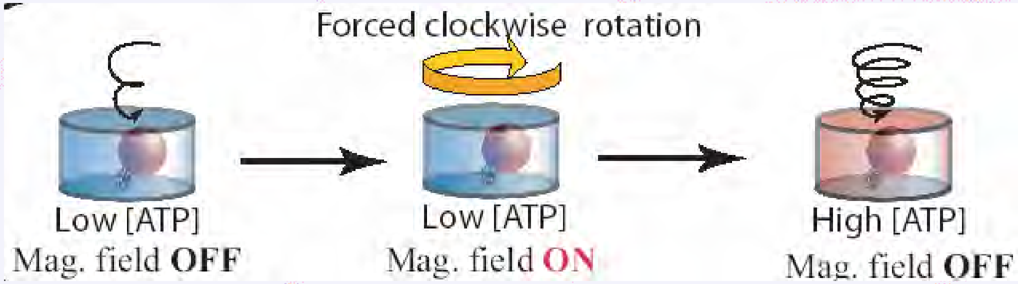
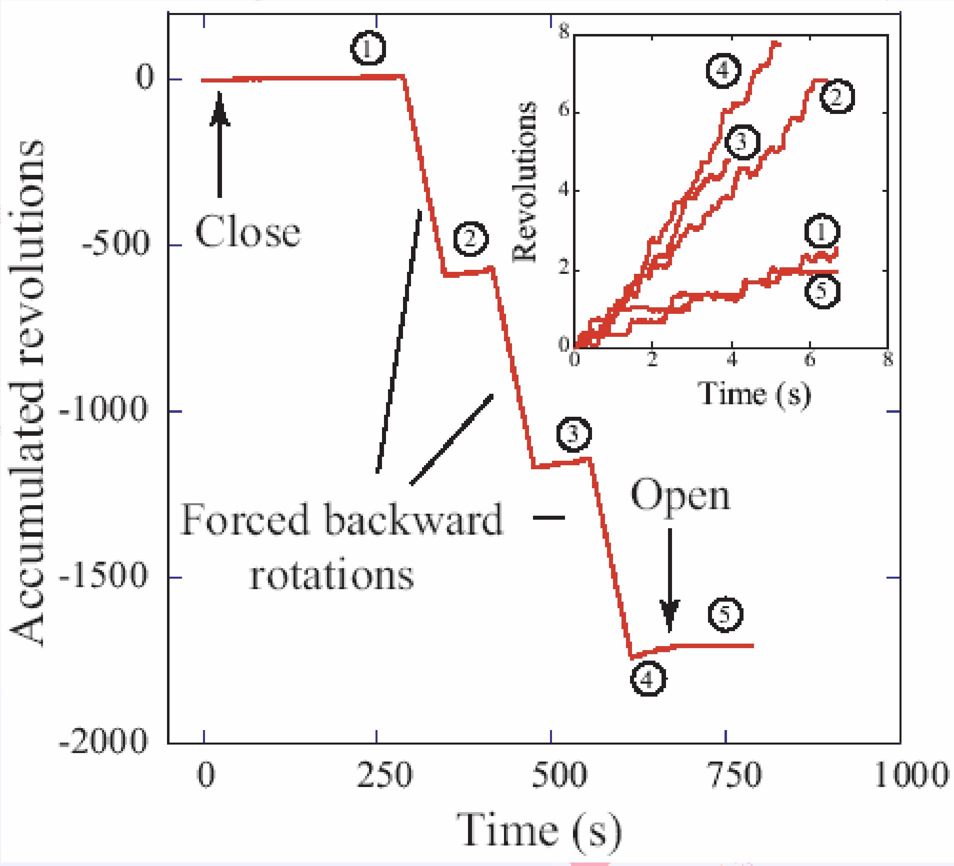
Single molecular measurement of ATP synthesis





Yannick Rondelez, et al.
Nature, 2005

Integration of microheater for characterizing protein denaturization by temperature control in *ms*

Hideyuki F. Arata, Frederic Gillot, and Hiroyuki Fujita

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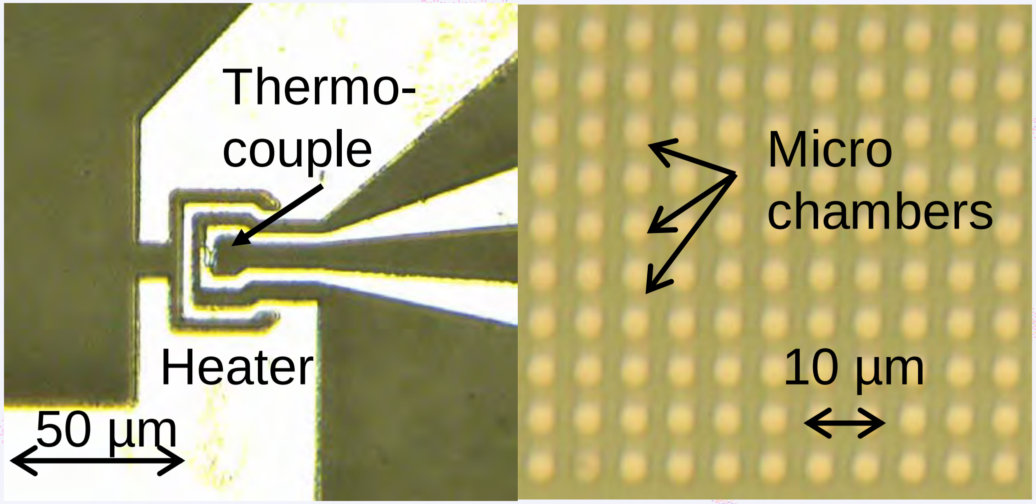
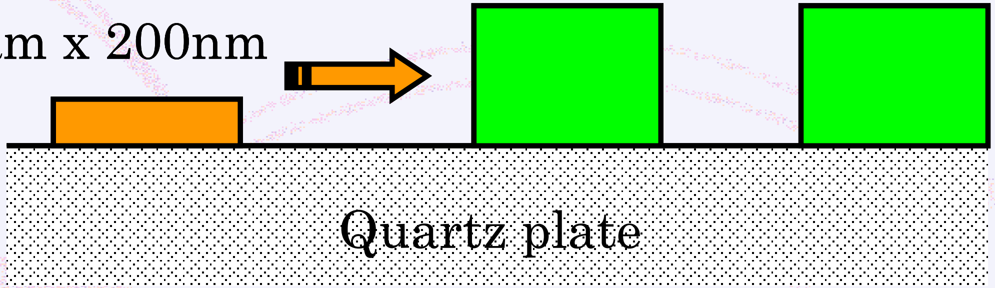
Micro heater with thermal sensor for quick temperature control



PDMS

Platinum Heater :
2µm x 200nm

Microcontainers:
ϕ3µm x 2µm



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H. F. Arata, et al. presented at Micro-TAS 2007

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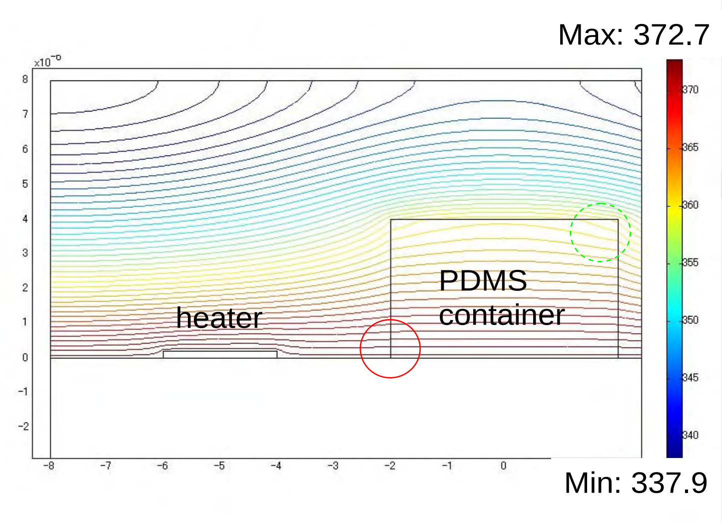
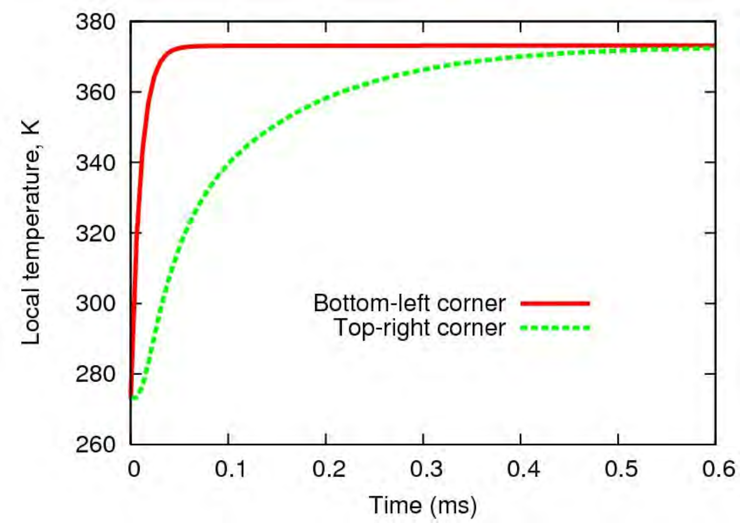
Simulation of spatial distribution and temporal change of temperature

Spatial temperature distribution at 20 ms after heater onset.



Transient temperature change at bottom-left corner (red) and top-right corner (right) of a microchamber. When the former reaches 373K, the delay for the latter to reach the same temperature was estimated to be ~0.6 ms.



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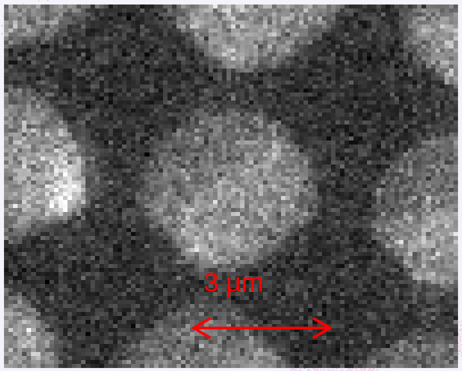
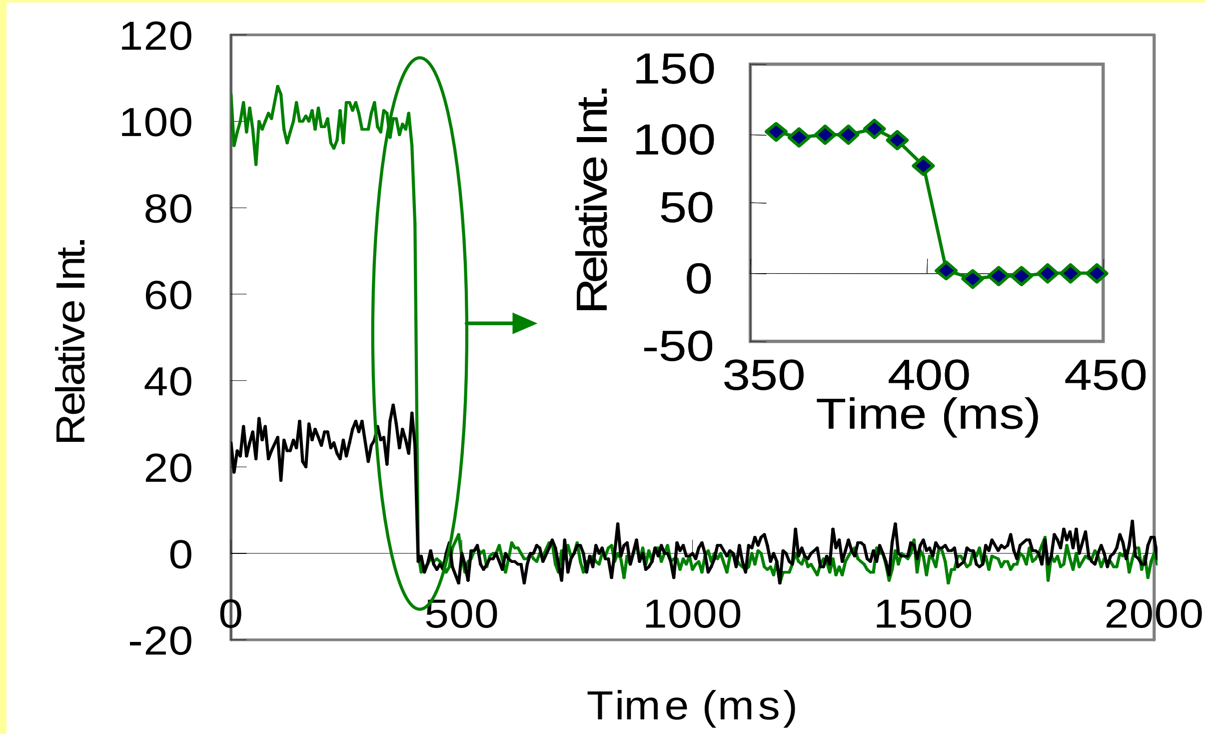
GFP characterization



Fluorescent view of GFP contained microchambers.



Time course of fluorescent intensity of a micro container (green) with that of background (black). The intensity decreased to the value of background noise by sudden temperature rise given by the micro heater.

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H. F. Arata, et al. presented at Micro-TAS 2007

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Content of talk

- MEMS
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- fL-chamber for confining molecules from diffusion
  - Single molecular analysis of F1-ATPase
  - Microheater for temperature control in ms
- Direct molecular handling
  - Molecular sorter driven by Kinesin-MT bio molecular motor.
  - Nano-machined tweezers for direct handling of DNA molecule.

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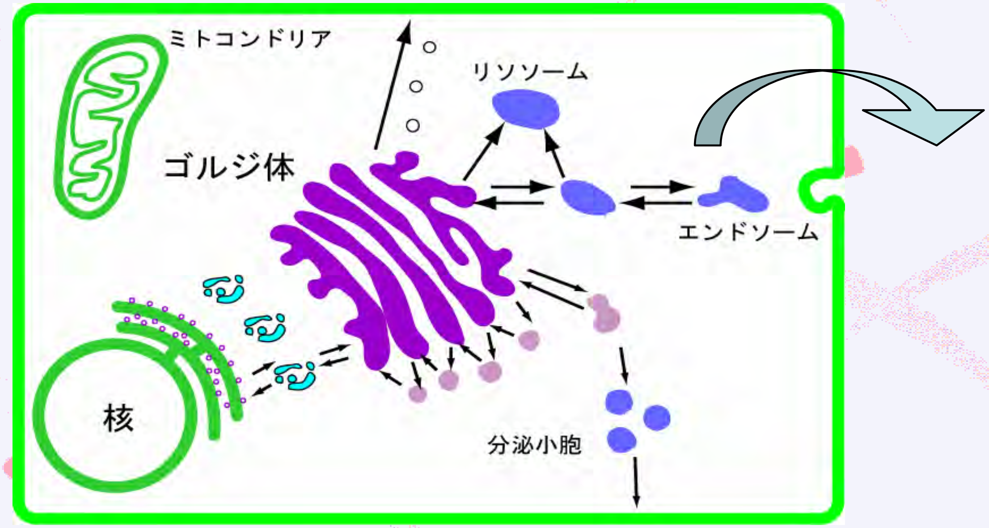
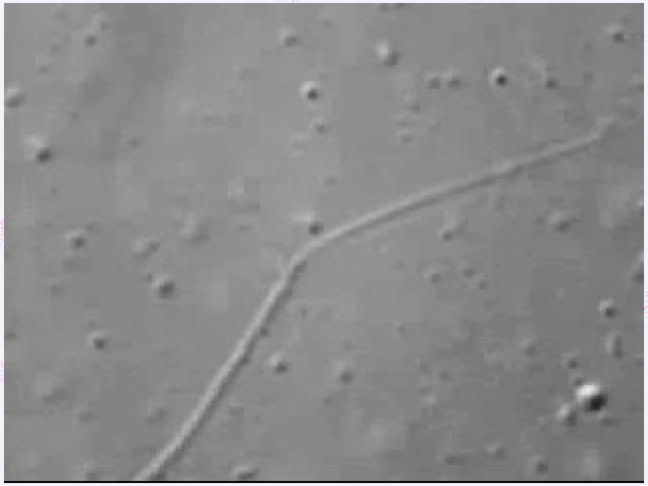
Intra-cellular conveyor driven by bio motors

Ryuji Yokokawa, M.C. Tarhan, Hiroyuki Fujita



schematic of cell inner structure



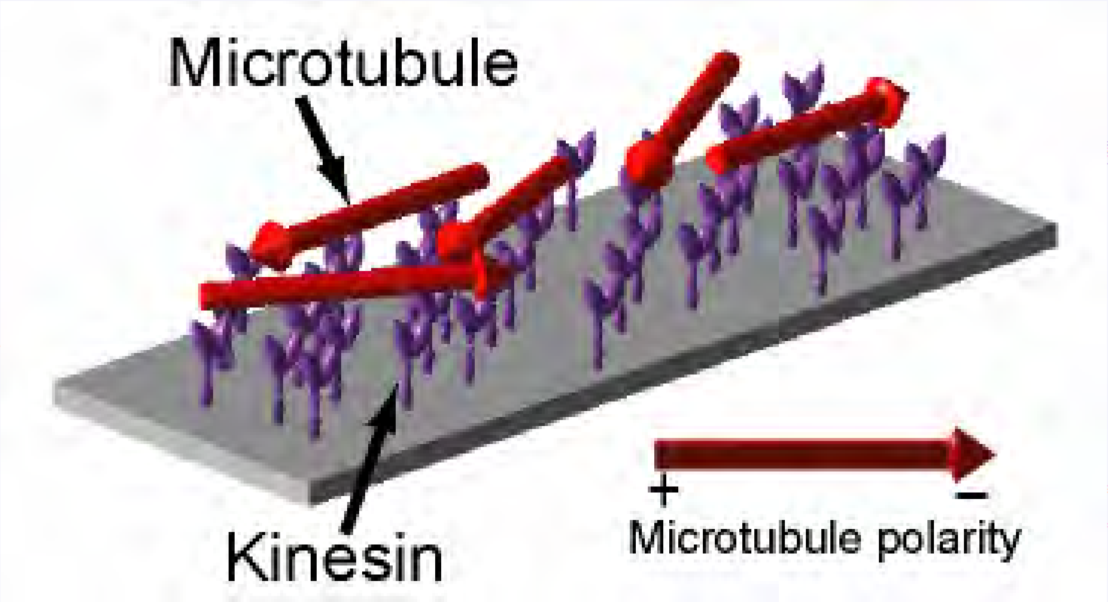
Issues to build nano conveyer

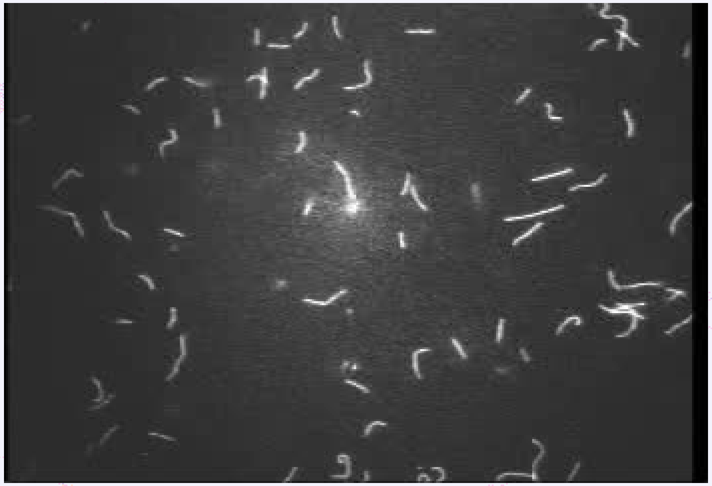
- Alignment of rail molecules
- Selective conveyance of targets
- Speed control

- Analogous to Shinkansen in Japan
  - Construct rail roads
  - Only allow ticked passengers to take trains
  - Stop at proper stations

Schematic of gliding assay

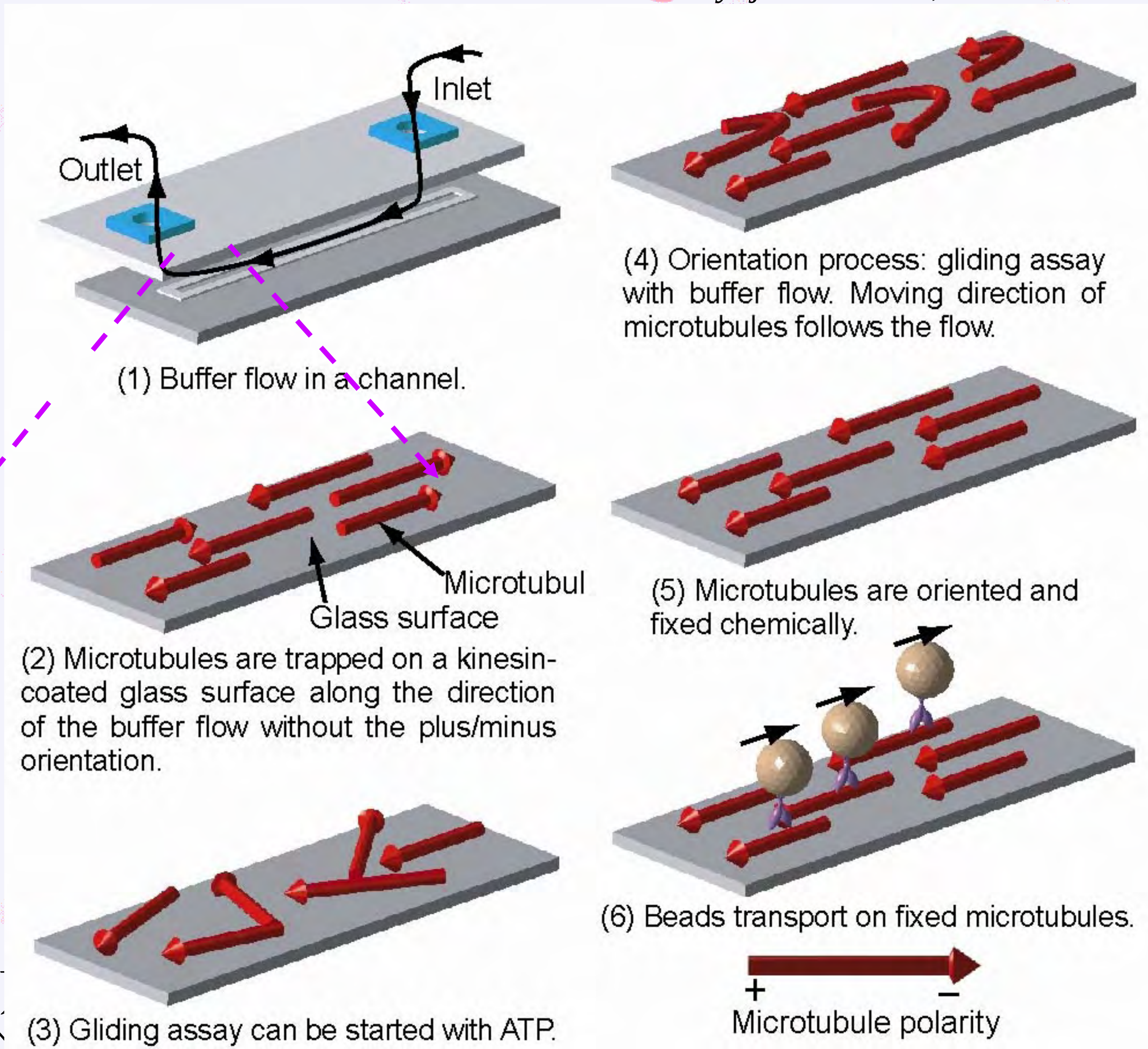
Microtubules are carried by immobilized kinesin on glass. The minus end towards which microtubule is transported is more easily removed by fluidic flow than the other end; this is utilized to align microtubules.





Unidirectional transportation (process)

Ryuji Yokokawa, et al. Nano Letter (2004)



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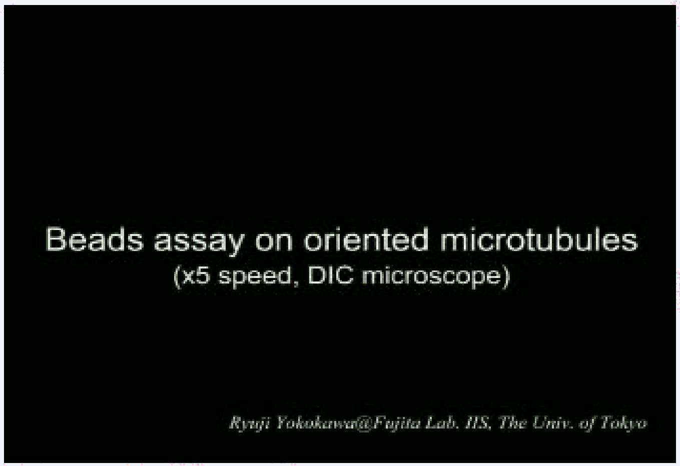
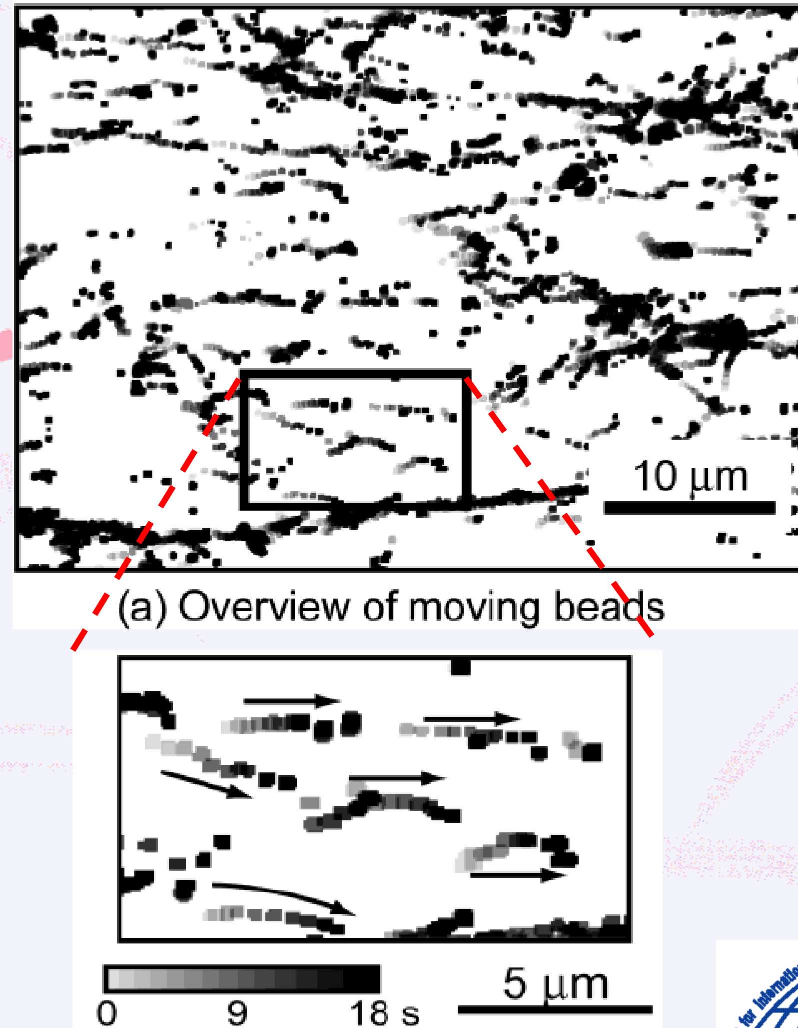
Unidirectional transportation (result)

Ryuji Yokokawa, et al. Nano Letter (2004)



90-97 % of beads moved toward the same direction.



(a) Overview of moving beads

(b) Closeup view

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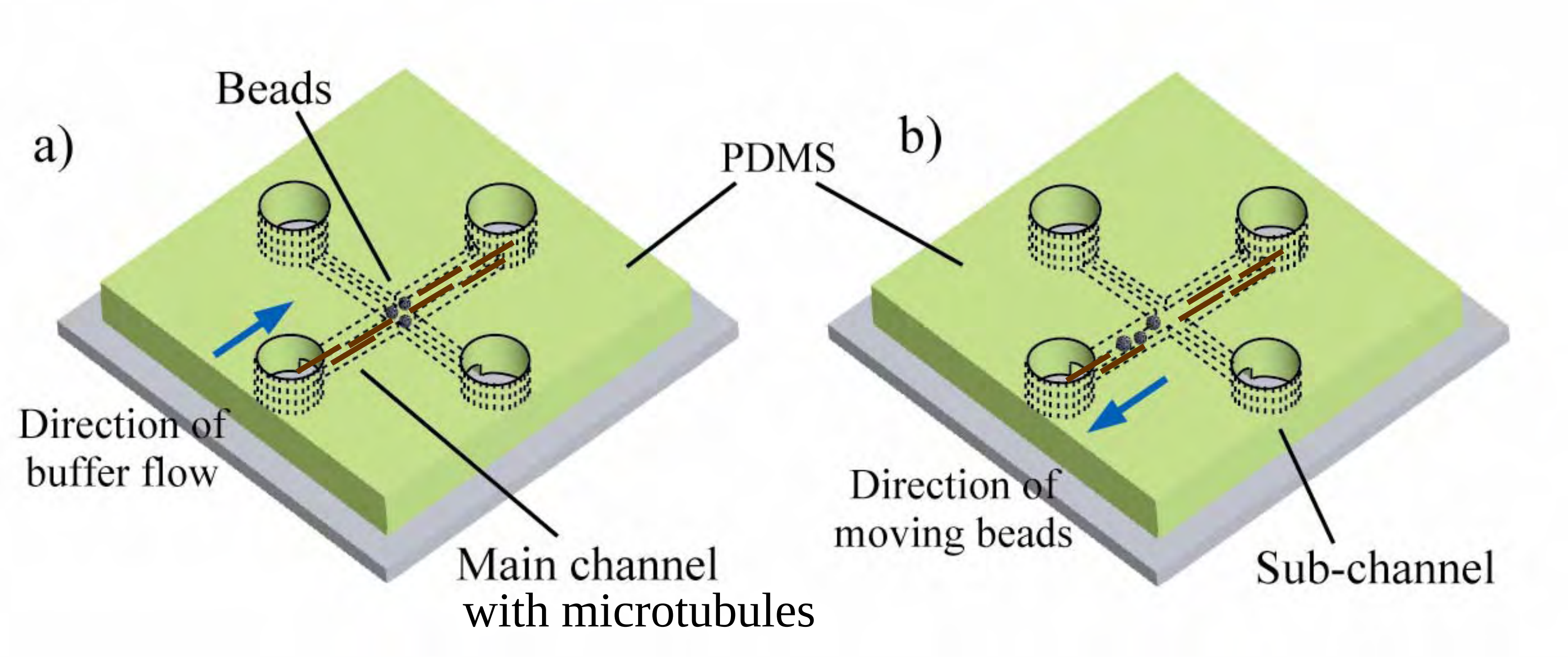
Transportation of target molecules

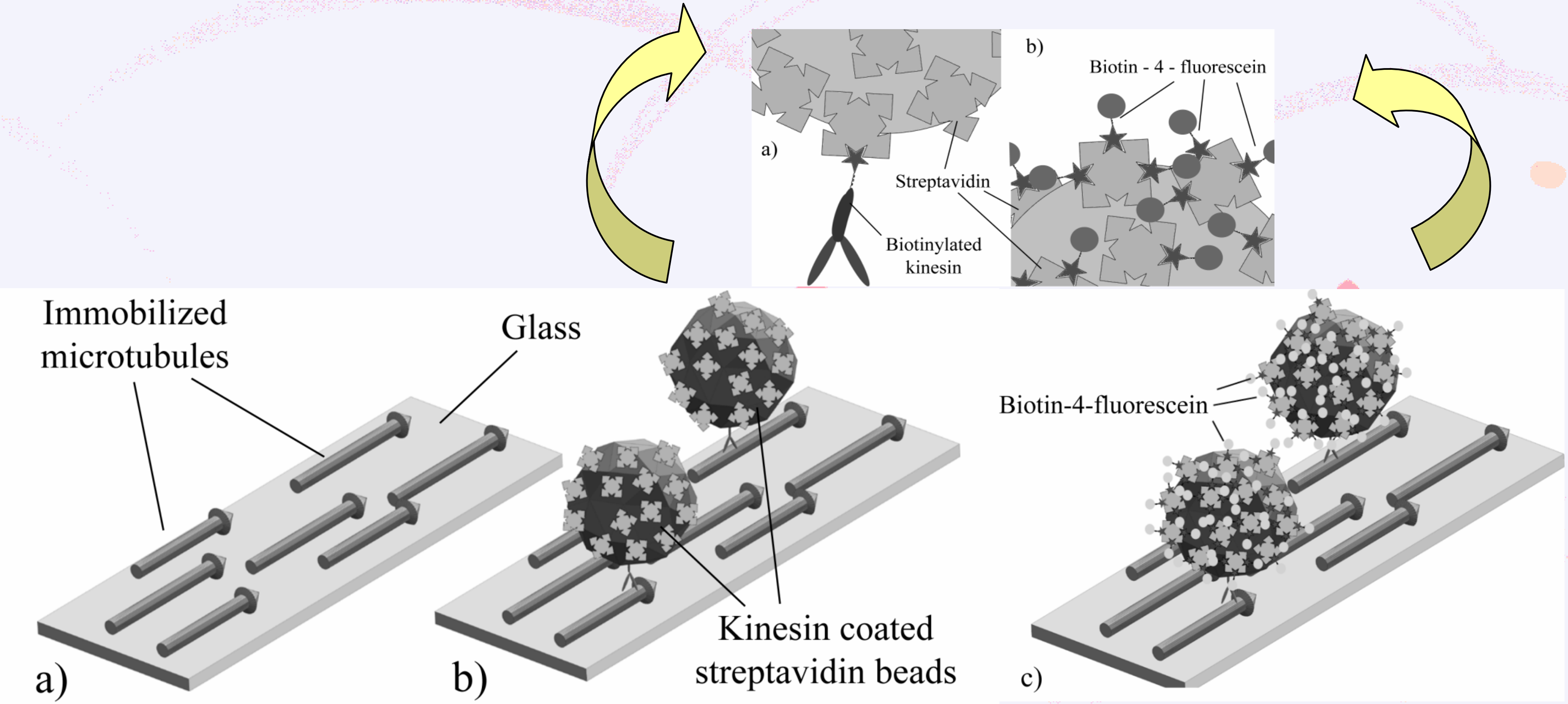
M. C. Tarhan, et al. IEEE MEMS-2006

a) Aligned microtubules are immobilized in the main channel. Beads are introduced from the sub-channel and attach to microtubules only at the intersection of both channels.
b) Target molecules are introduced from sub-channel and are captured by beads. After washing, ATP introduction to main channel starts the transportation of beads with target molecules.



Selective attachment by avidin/biotin pair

M. C. Tarhan, et al. IEEE MEMS-2006



We have added another pair (Protein-A and its antibody).
Each type of molecules are conveyed on its corresponding beads.

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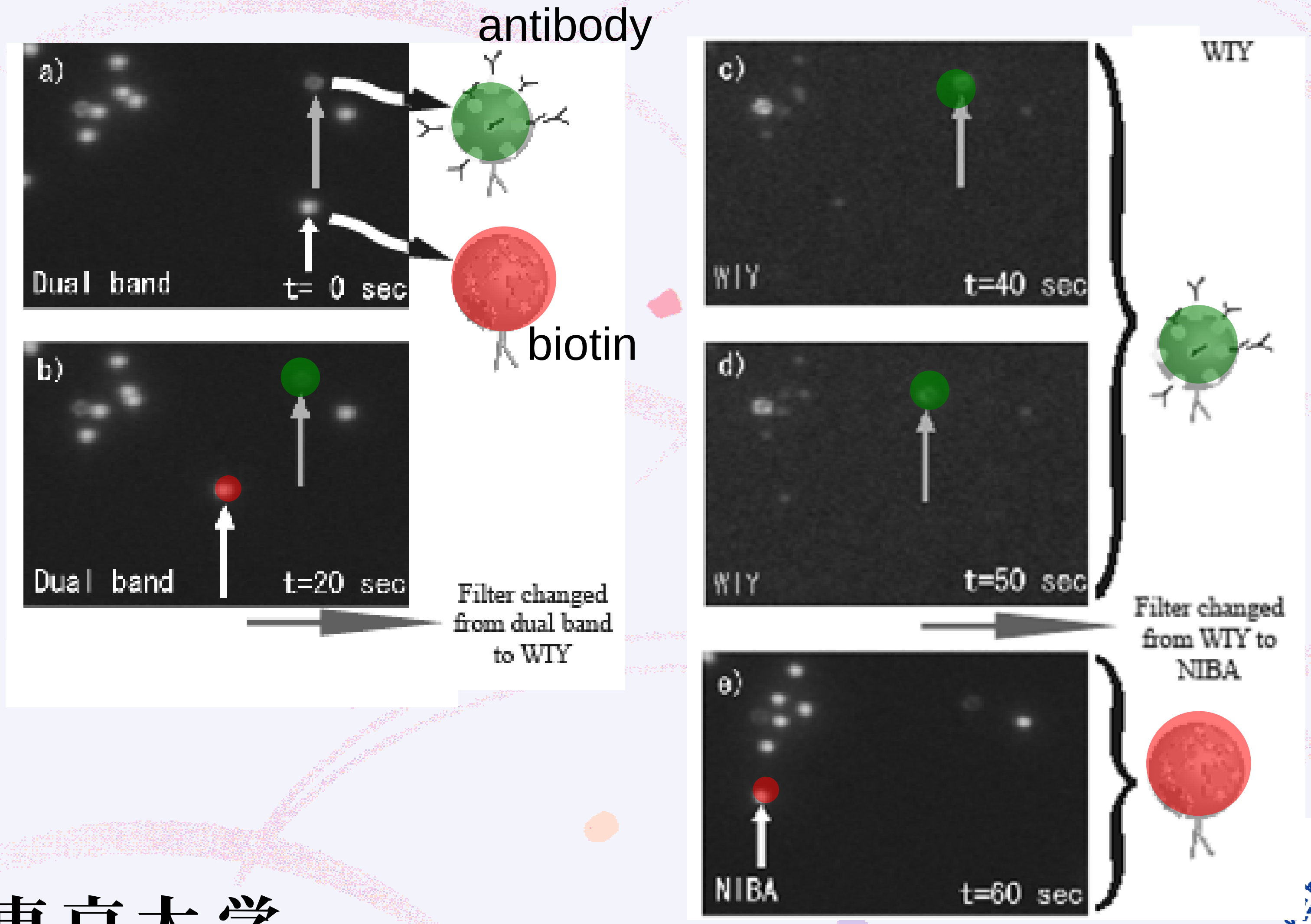
Selective transportation of target molecules

M. C. Tarhan, et al. presented at IEEE MEMS-2007



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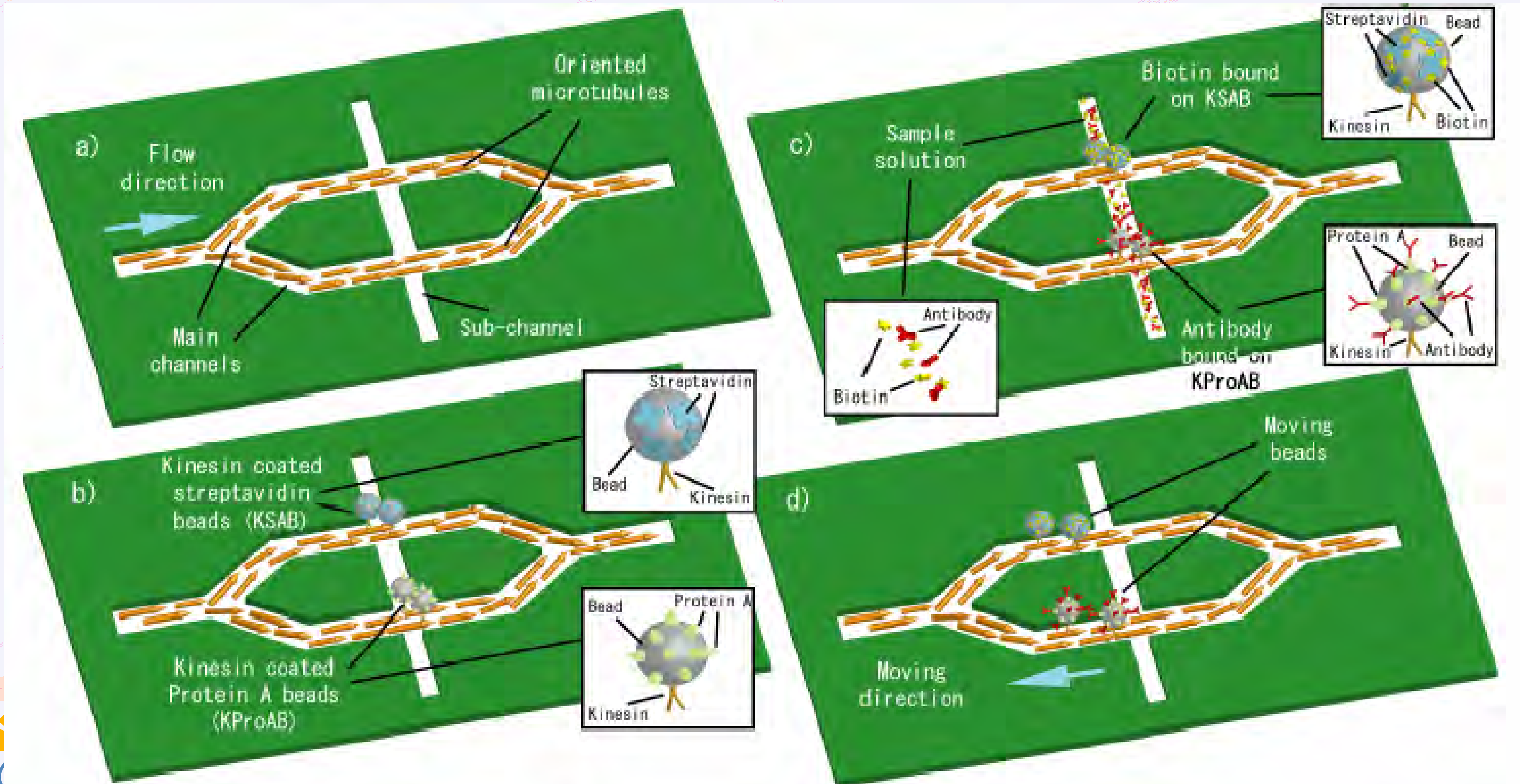
Selective retrieval of molecules by molecular recognition and direct transportation by bio molecular motors was achieved.

M. C. Tarhan, et al. IEEE MEMS-07



Conclusion

- Progress in MEMS and microfluidic devices has enabled advanced single biomolecular analysis.
- MEMS enabled advantages:
  - confinement of molecules in fL-chamber
  - Temperature control in milliseconds
  - Reconstruction of cellular parts
  - Direct handling of bio molecules (down to single molecular level)
- MEMS characterization tools for nano/bio technology are promising.

Acknowledgment

- COE-21 Program
- MEXT
- JST
- JSPS
- CNRS (France)

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In collaboration with

- Professors affiliated with CIRMM
  - Hideki Kawakatsu, Hiroshi Toshiyoshi, Dominique Collard, Teruo Fujii, B. J. Kim, Shoji Takeuchi, Yasuhiko Arakawa, Alan Bossebeouf, Yasuyuki Sakai
- Prof. Masao Washizu
- Students, post-Docs and visiting scientists
  - Mr. E. Altintas, Mr. M.C. Chagatai, Dr. H. Sakaki, Dr. Momoko Kumemura, Dr. C. Yamahata, Dr. Y. Rondelez, Dr. K. Kakushima
- Japanese partners
  - Prof. Hiroyuki Noji (Osaka Univ.) and his group
  - Prof. Gen Hashiguchi (Kagawa Univ.) and his group
  - Prof. Ryuji Yokokawa (Ritsumeikan Univ.) and his group
- Global partner
  - Prof. Karl Boeringer (U. Washington)
- And many others…

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