# Advancements in SPM instrumentation for bio-applications

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# Outline

- Introduction
- Non Contact AFM
- SICM
- Conclusions



#### AFM





# Advantages of AFM

- High Resolution: ~nm lateral, <nm vertical</li>
- Quantitative 3-D information
- Operates in air, liquid, and vacuum
  Ability to study in physiological buffer
- Does not depend on electrical conductivity
   No requirement for Au/Pd or C- sputter coating
- Can measure mechanical, electrical, optical, and other physical properties
- Manipulation of specimen in nanometer scale



# Microscopy in Biology



## **Common Problems in Conventional AFM**

- +V = V
- Piezo tube is not an orthogonal 3-D actuator
- Non-Contact Mode not possible due to Slow z-servo response



Even after software flattening, flat surface does not "look" flat.





## **AFM Technology Innovation**



Single module parallelkinematics x-y scanner

- Independent z scanner from x-y scanner
- Precision Nanometrology
- True Non-Contact AFM





#### Tapping vs. True Non-Contact Mode



# Microscopy in Biology



#### DNA



#### **Plant Virus**



## Spontaneous assembly of Viruses on multilayered polymer surfaces



### Bacteria as Chemical Factories





- vitamins
- therapeutic agents
- pigments
- amino acids
- viscosifiers
- industrial enzymes
- PHAs (biodegradable plastics)



## PHAs (Polyhydroxyalkanoates)



## **Complex Structure of Cell Membrane**





## Imaging the Inside of Cell Membrane





## TEM image of Hela Cell Inside (8µm)



#### AFM image of Hela Cell Inside



#### In-Liquid, NC-AFM

Sample provided by Jiro Usukura



## AFM image of Hela Cell Inside



Sample provided by Jiro Usukura

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### **Clathrin Coated Vesicle**

#### In-Liquid, NC-AFM



Model



Sample provided by Jiro Usukura



## Imaging the Muscle Fibers





## Imaging the Muscle Fibers

In-Liquid, NC-AFM



#### AFM (5 × 5μm)

By Noemi Rozlosnik



TEM



#### F-d curves on Muscle Fibers



### Collagen Fibers from the Connective Tissue



# NSOM/SICM



### Exchangeable SPM Heads for Bio Imaging



#### $25 \mu m \ AFM \ HEAD$

Optical HEAD for NSOM & Raman

SICM HEAD



## NSOM: Kidney Cell (293 T)

AFM Topography

#### NSOM image



Excellence in Nanometrology

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## Scanning Ion Conductance Microscopy











# Scanning Ion Conductance Microscopy





## Scanning Ion Conductance Microscopy



#### **Distance-modulated Control**



#### SICM of Live Cell: C2C12(mouse muscle)



Topography

Current



## Mechanical Stimulation with a Nanopipet





### "Smart" Patch-clamp



#### Multi-Component Graded Deposition of Biomolecules with a Multi-Barreled Nanopipet



# Microscopy in Biology



# **Biological Applications of SPM**

- Biological Sample Imaging
  - Cell
  - Membrane & Membrane Protein
  - DNA
- Molecular Interaction
  - Protein-protein interaction
  - DNA-protein interaction
  - Cell to cell interaction
  - Single-molecule force spectroscopy
- Biological system dynamics
  - Cell dynamics
  - Vesicle dynamics
  - Phase transition of phospholipid membrane
- Manipulation
  - Biomolecular nanolithography (protein, nucleotide)
  - Bio-Manipulator

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## Conclusions

- SPM is a very powerful tool for nano-bio science and technology.
- The new generation AFM with true Non-Contact mode was developed.
- SICM is becoming the new driving force in the field of nano-bio science.

