

# Application of bio-nanotechnology in Chinese medicines

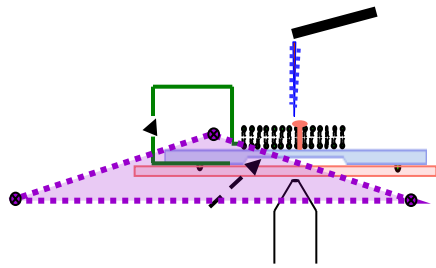
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Co-Director, Center for Excellence in Nanomedicine and Engineering, IEM  
University of California, San Diego  
Visiting Professor, Chinese academy of Sciences

**Seminar on Research and Development of Chinese Medicine**  
Hong Kong Convention and exhibition Center  
Hong Kong

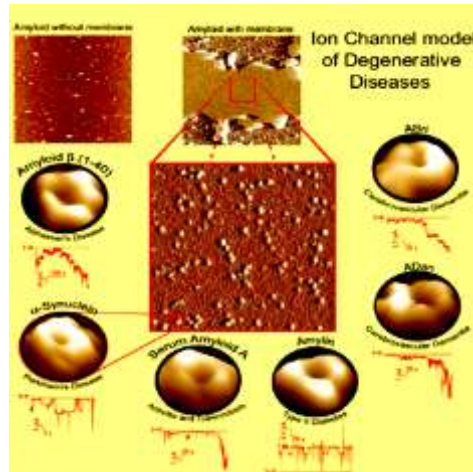
September 10-11, 2015

# Nano-Bio Lab



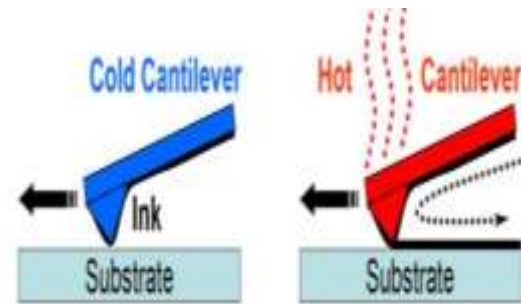
## Nano biotechnology

- Nanoimaging
- Nanomanipulation
- Nanopatterning
- Nanoarray design and synthesis



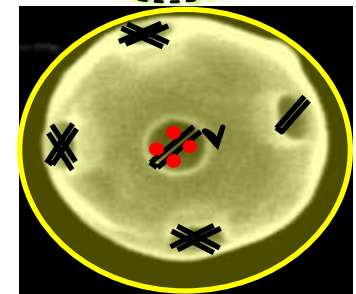
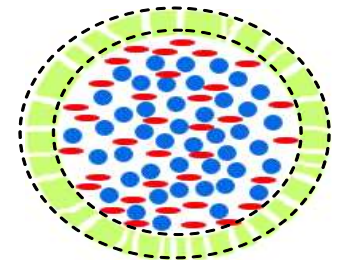
## Imaging-based Diagnostics

- Amyloid diseases
- Heart diseases
- cancer



## Nano-machines and sensors based on:

- Cantilevers
- Nano chips
- Smart materials to sense forces, fields and energies



On-demand, targeted delivery

Today Talk: Can Nanotechnology help Chinese Medicine get Global acceptance

# Nanoscience and technology is about

- **Understanding principles of physical world**
- **Designing Technology to unravel world**  
at the scale of molecules and structures that  
make and run the world we live in

## Beginning of Nanotechnology and Nanomedicine

### • **Discovery of Nanotube**

- Nanoscale materials with magical properties for interactions with its environment

### • **Discovery of Scanning Tunneling and Atomic Force Microscopes (STM and AFM)**

- Allow study of structures, motion and all physical forces at atomic scale in fluid
- Allow manipulating and creating structures at atomic scale

# Accelerating Nanotechnology Applications to Human Health - Nanomedicine

- **Global Population:  $>10^9$**
- **Human size:  $10^0$**
- **Human cells:  $10^{-6}$**
- **Biological macromolecules:  $10^{-9}$**
- **Biological processes:  $10^{-11}$ - $10^1$**
- **Which means billions of us are controlled by structures and mechanics billionth times smaller (Nano) than us**

- **Global Investment:  $>\$10^{10}$**
- **Current Global market:  $\sim\$10^{10}$**
- **Global market by 2017:  $\$10^{12}$**
- **Global Nanobio companies:  $\sim 10^3$**

- **Disease Diagnosis:  $10^1$**
- **Disease Treatment:  $10^1$**
- **Disease Prevention:  $10^1$**

**Can TCM gain a larger share of the market?**

**Define Targets**  
Receptors, Channels

**Design Therapeutics**  
Drugs, interventions

**Define cause and  
Diagnose Pathology**

## **Scope of Nano-biotech & Nanomedicine**

**Targeted Delivery**  
•Controlled delivery,  
•guided delivery  
•On-demand release

**Monitor Disease  
And  
Therapy states**

**Devices to Maintain  
Tissue Activity**

**Optimize Efficacy  
Minimize Side Effects**

**Devices for Tissue regeneration**  
•Stem cell therapy  
•Wound healing  
•Bone growth

**In-vivo Sensors**  
• Diagnosis  
• Remotely controlled  
• Multi-functional

### **Diagnosis:**

- high resolution and
- sensitivity

- Biocompatible/non-toxic
- in Vivo Stability
- biodegradable

### **Therapy**

- Reduce the Dose
- Treat localized cells/tissues
- Minimize side effects

# I will give examples of nanoimaging, nanomaterials and nanomechanics technology that relates to three essential components of all living systems (structure, motion and interaction with environment) can be used in Chinese medicine

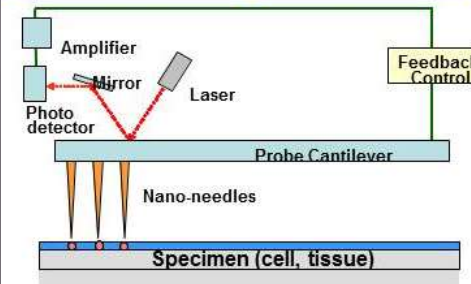
➤ Holistic Approach

➤ Medicine works by the synergistic action of many active constituents

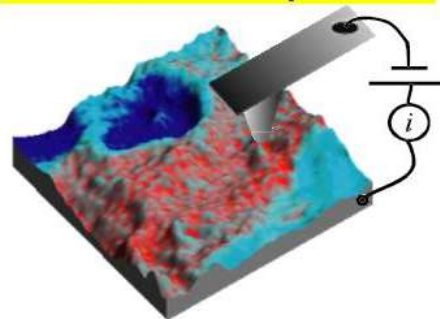
Topics	No. of Publications
Nanotechnology in Medical Applications	295,000
Chinese Medicine	2010
Homeopathy	652
Ayurveda	644
Acupuncture	849
Acupressure	49
Japanese Medicine	5
Korean Medicine	10

**Nanotechnology in Eastern Medicine (<1%)**

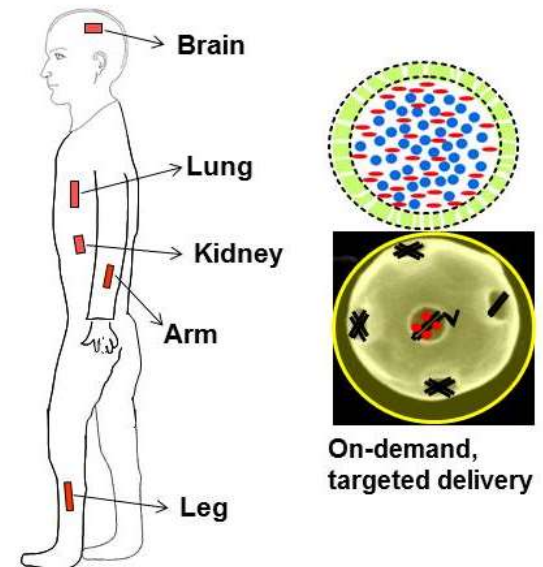
## Nano-acupuncture



## Nano-electro-acupuncture



## Delivering Chinese medicine to specific organs



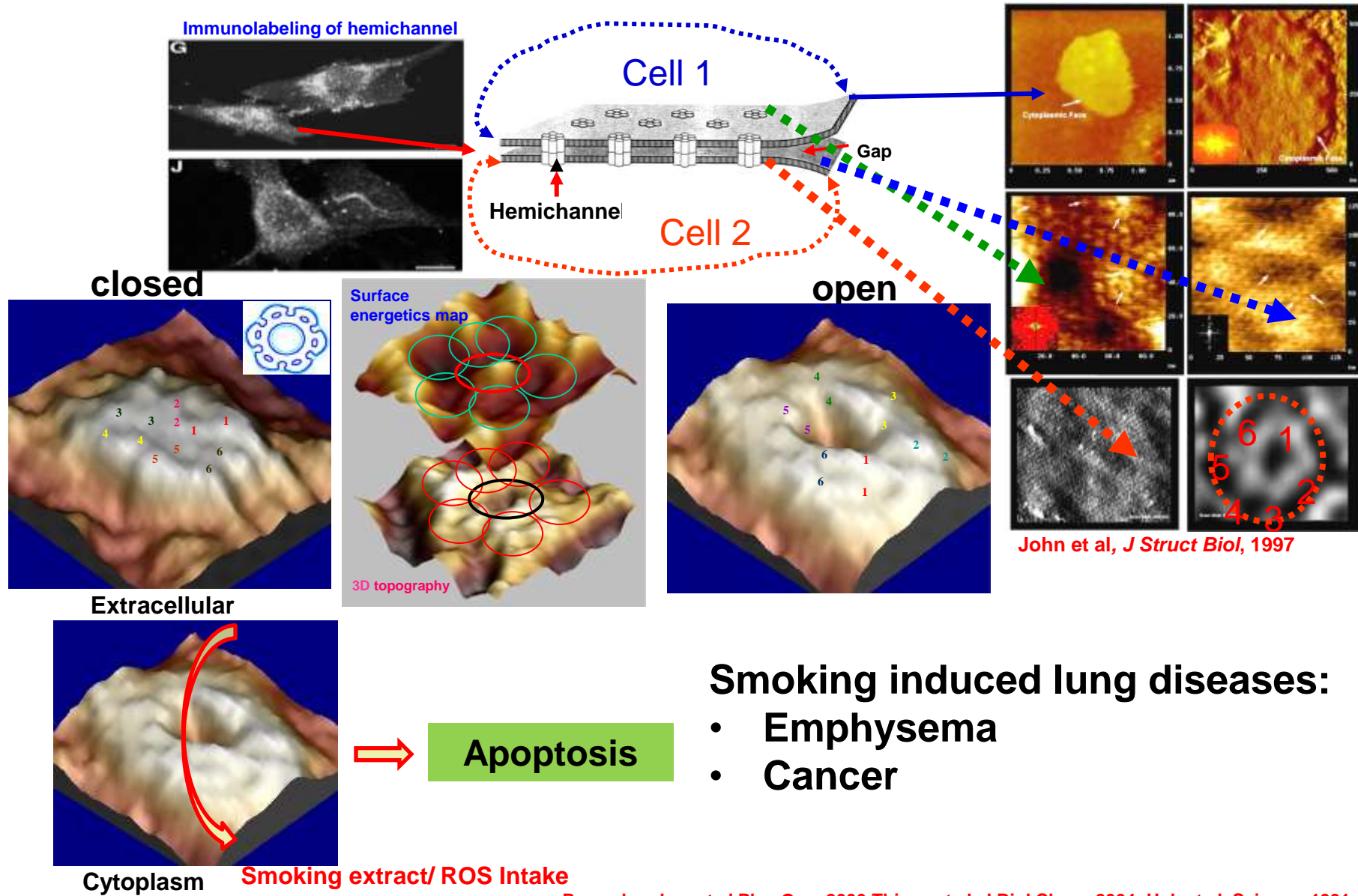
# Nanoimaging for Nanomedicine

- **Imaging functional ion channels**
- **Imaging amyloid (misfolded) channels**
- **Imaging single molecule proteolysis**

**Relevance to Heart and lung diseases,  
Alzheimer's and other brain diseases,  
muscular diseases, cancer**

# Cell-Cell and Cell-Surround Communication Channels

A key Structure for the Evolution and Sustenance of Multicellular Organisms





# Good and Bad of Amyloids

## • Amyloids as Foe

Protein  
Misfolding



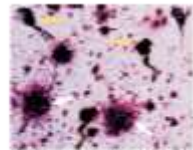
Amyloid  
Proteins



Accumulation  
as PLAQUES



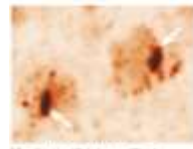
Cell Death, Disease  
and System Failure



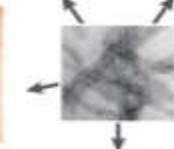
Alzheimer's plaques and tangles



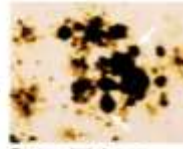
Parkinson's Lewy bodies



Huntington's intranuclear inclusions



Amyloidotic renal sclerotic aggregates



Prion amyloid plaques



Amyloidotic renal sclerotic aggregates

- Nervous system
- Immunity
- Metabolic
- Transport

## • Amyloids as friend

Infection



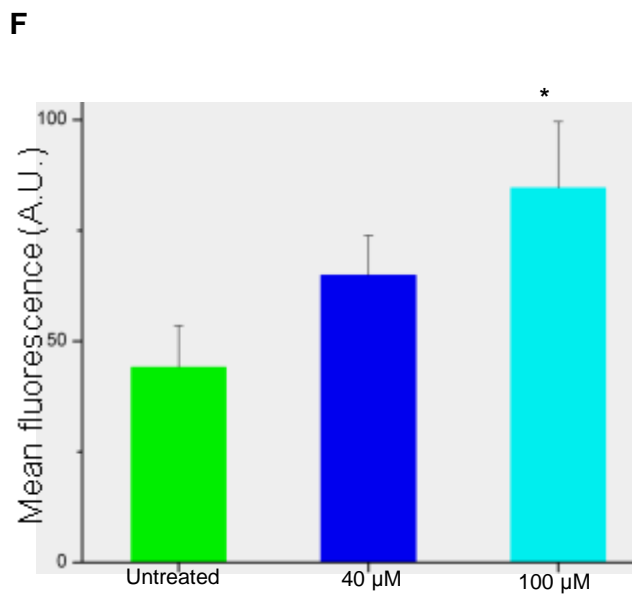
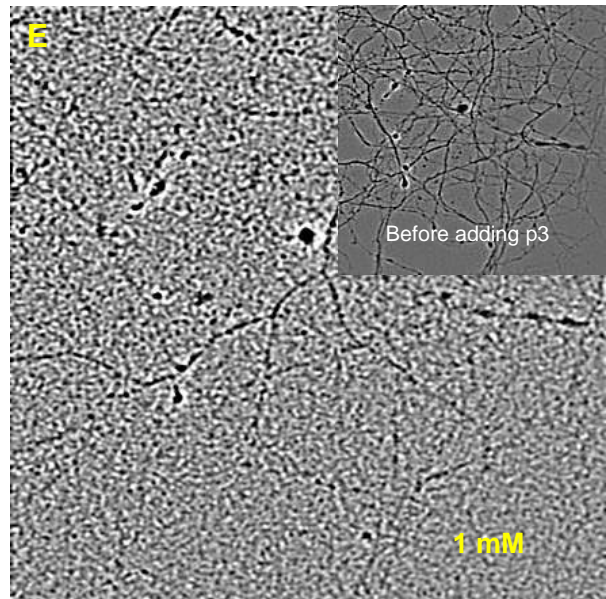
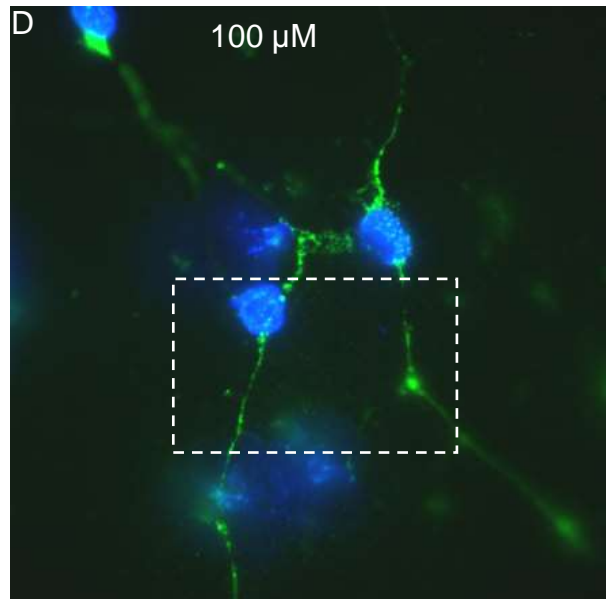
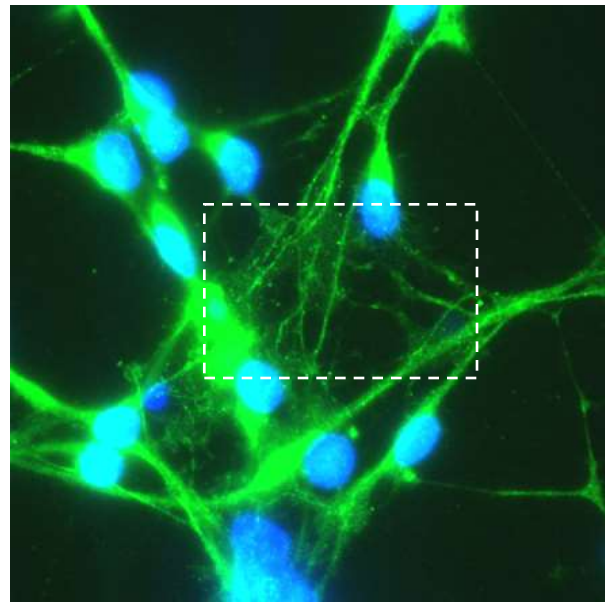
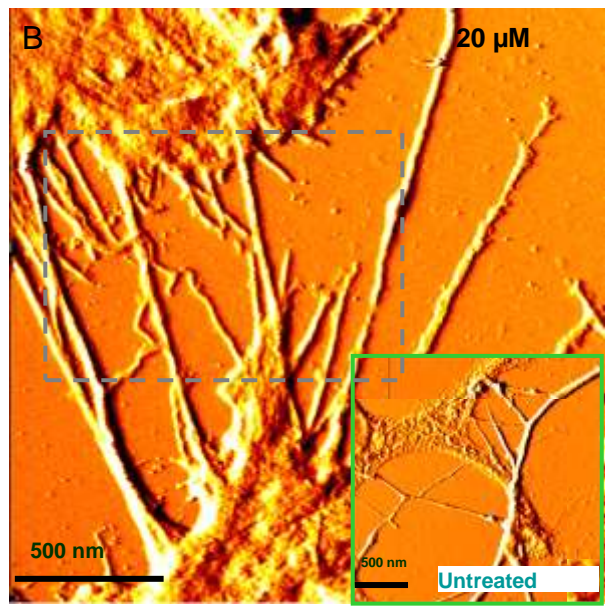
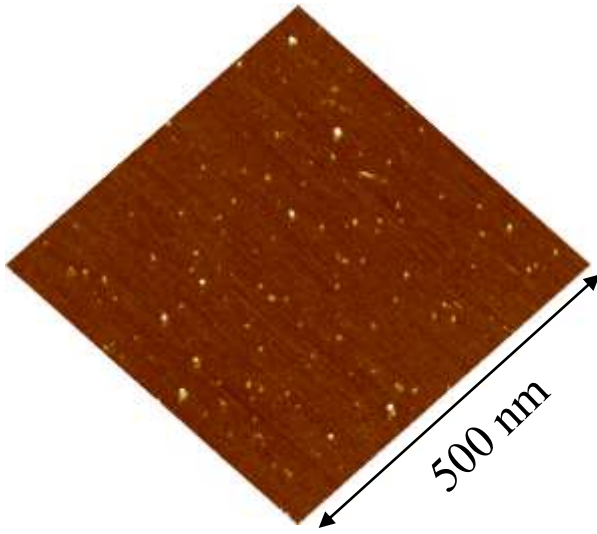
Amyloid Proteins  
(Anti-microbial Proteins)



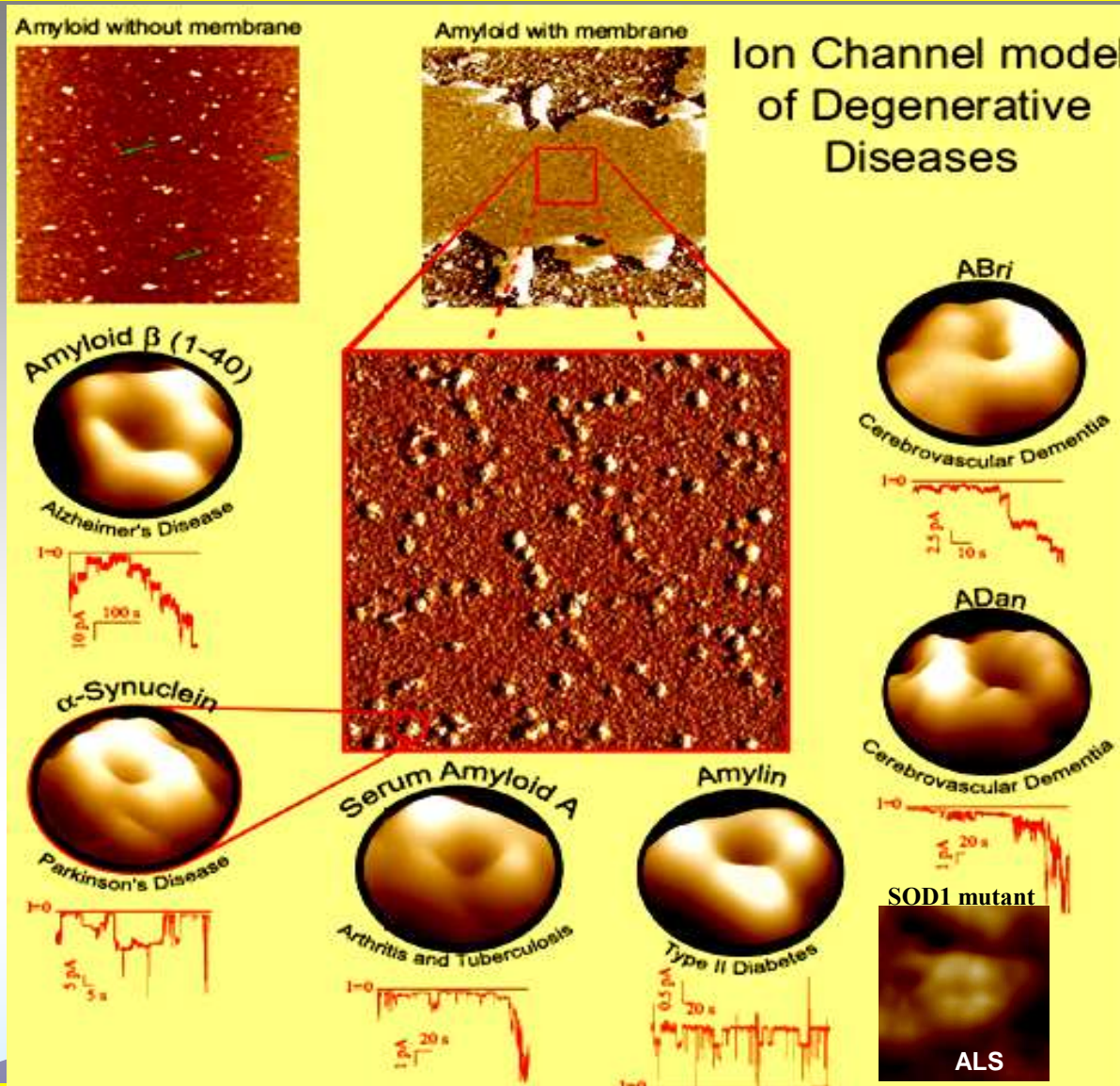
Death of infecting  
agents

Is plaque, fiber or oligomer the mediator?

# Amyloid peptides Induce dose-dependent synaptic degeneration



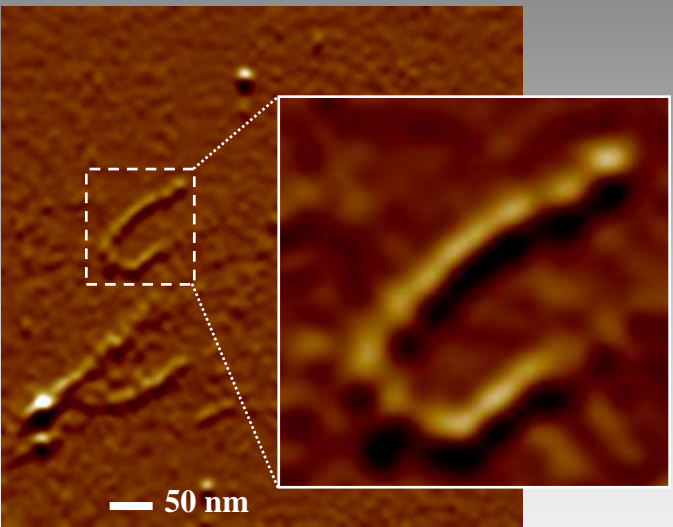
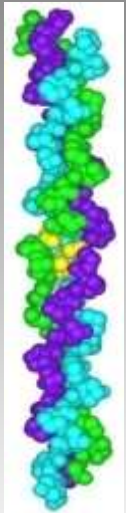
# Defining New Paradigm of Disease Process And Defining Target (Channel/Receptor) Structure



**Amyloid Diseases are a class of "Channelopathies" with Defined Ion Channels**

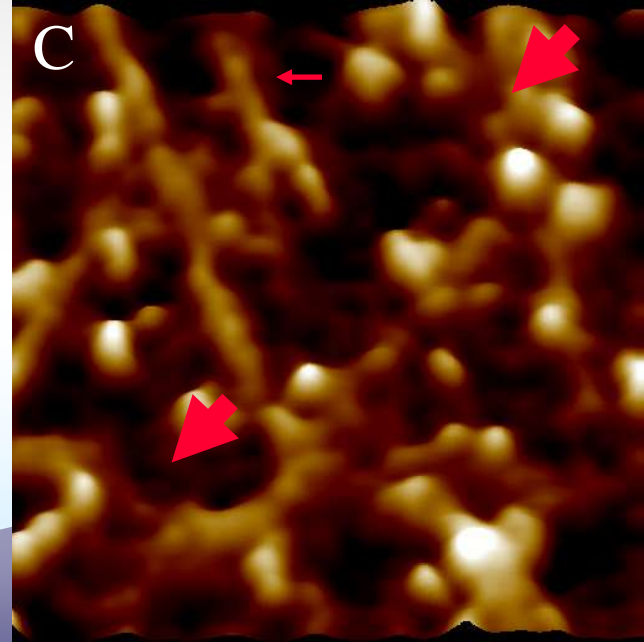
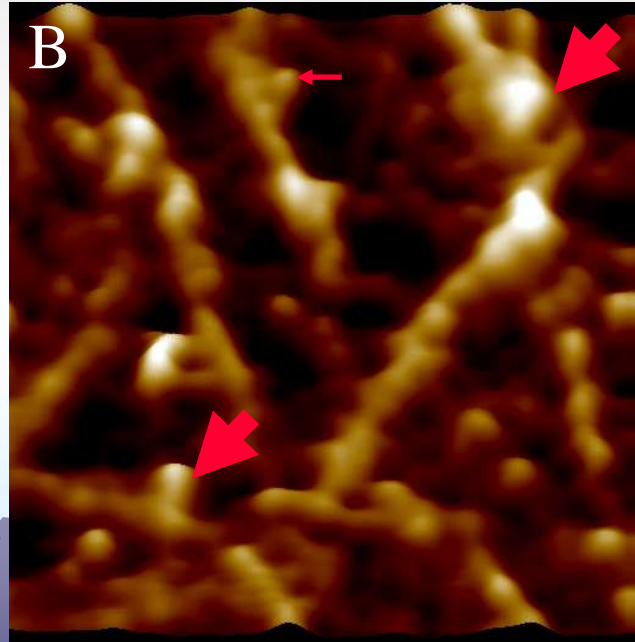
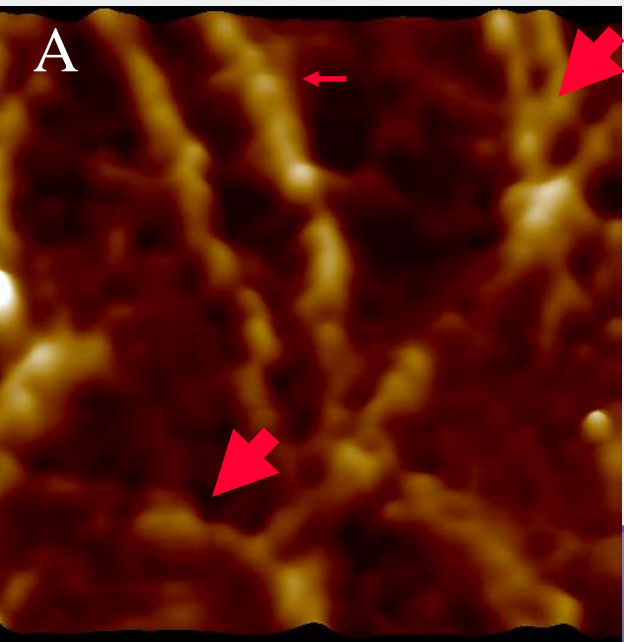
# Real-time collagen-collagenase Association-dissociation

## Defining Therapeutics' Efficacy and Dosage



Single triple helical collagen I molecule: AFM image

A key Extracellular matrix protein, provides support for tissue sustenance and growth



# Nano-mechanics for Nanomedicine

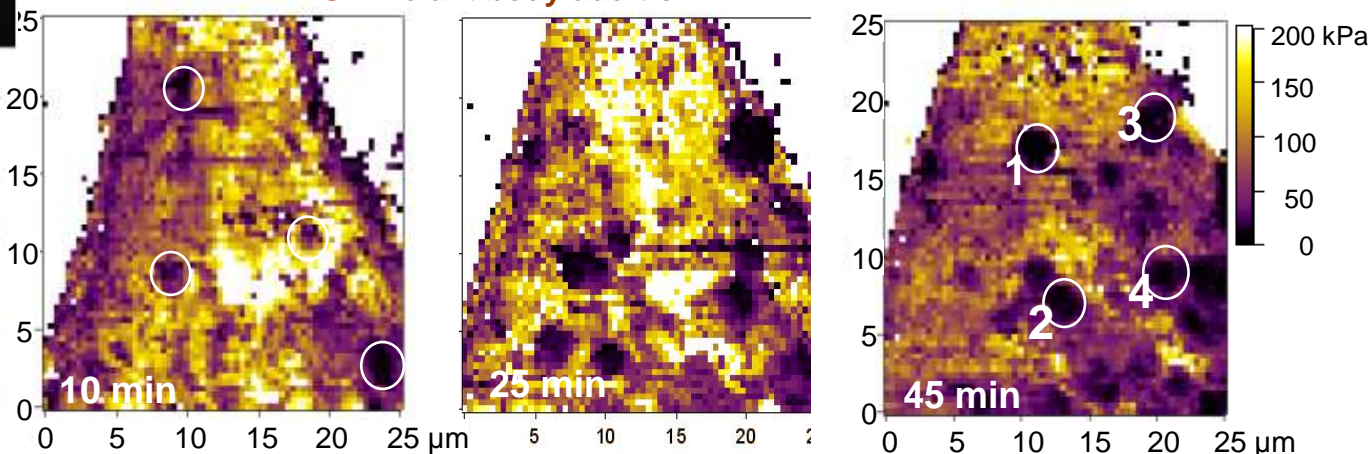
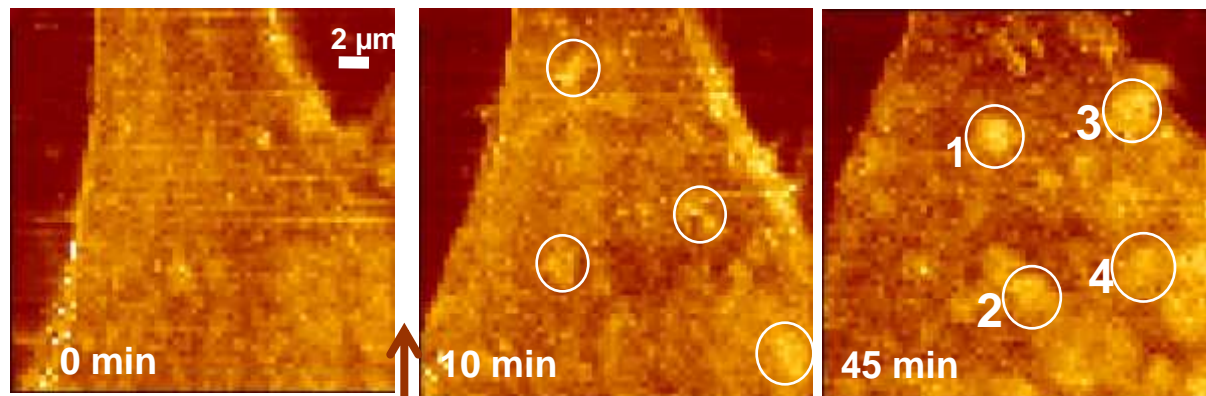
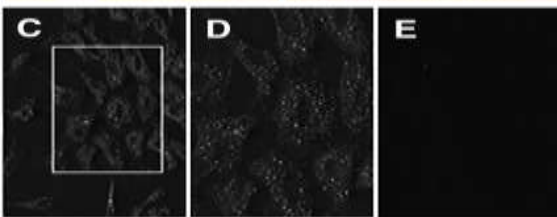
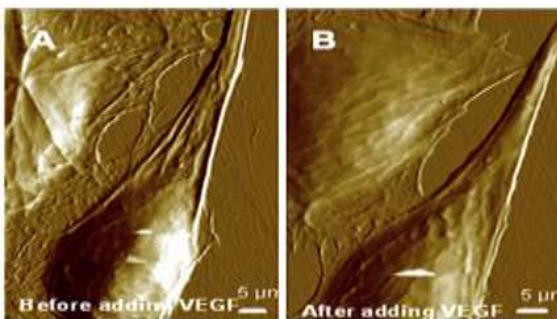
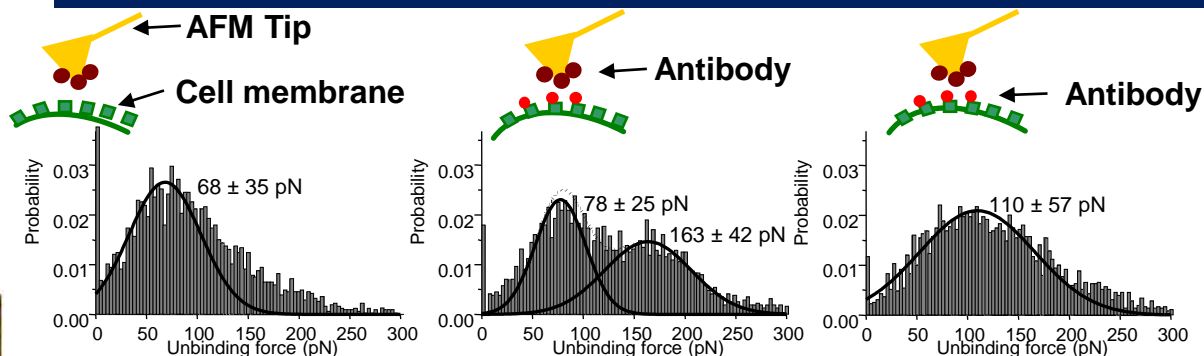
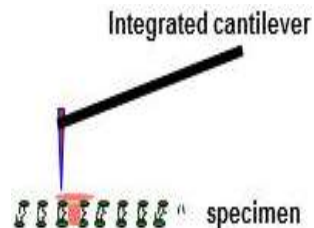
- Sensing intermolecular interaction
- Sensing intracellular mechanics
- Sensing whole cell mechanics
- Sensing tissue mechanics
- Sensing composite materials mechanics
- In-vitro sensors for Biomarkers
- In-vivo Sensors for Biomarkers and therapy

**Diagnostics, Designing therapeutics and  
Therapy monitoring**



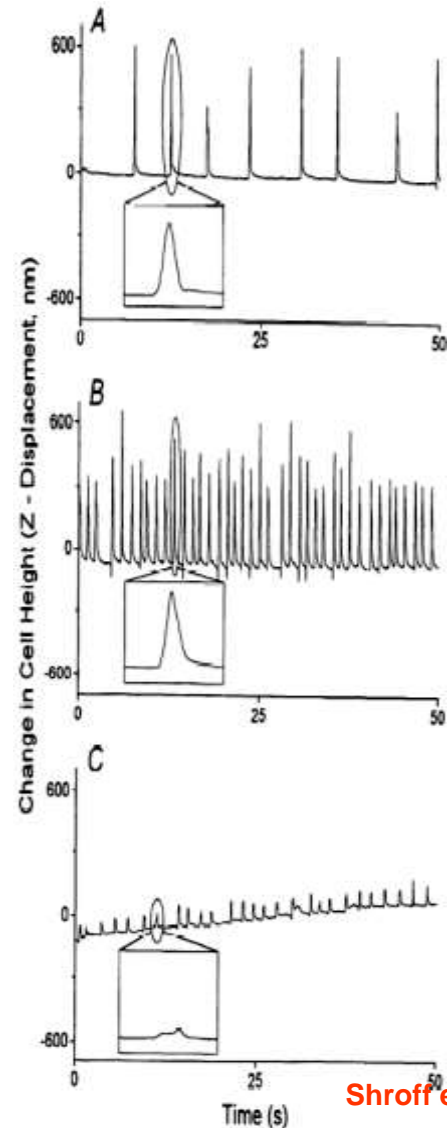
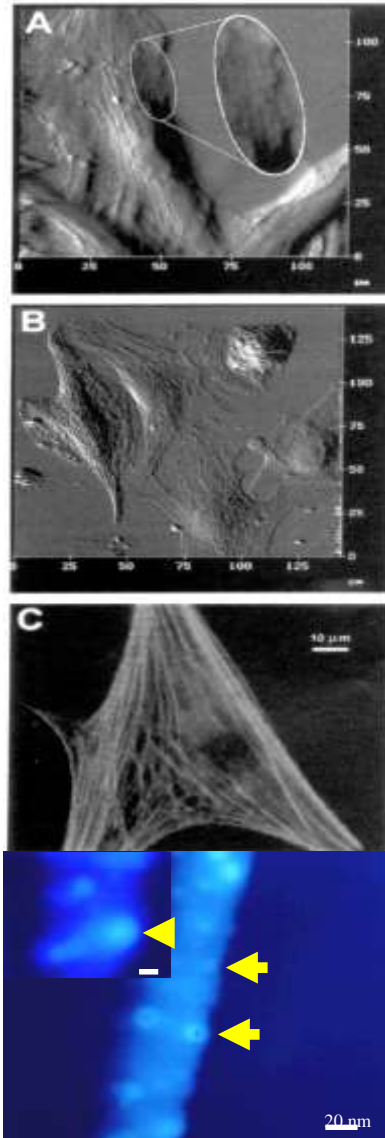
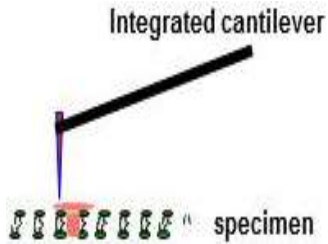
# Single molecule spectroscopy on living cells

## Locating Therapeutic Targets: VEGF Receptors



# Nanomechanics of a Pulsating Muscle Cell

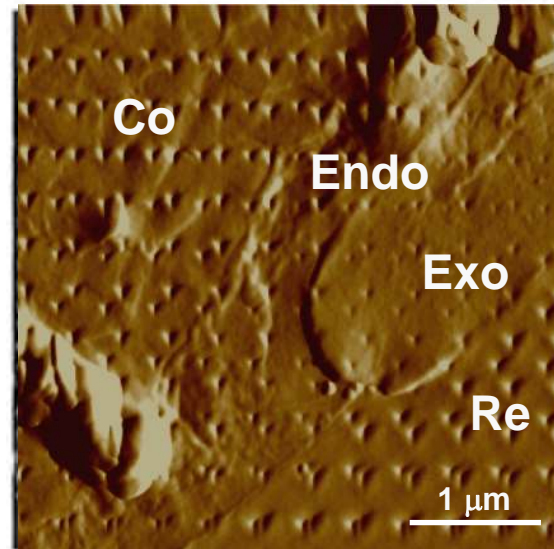
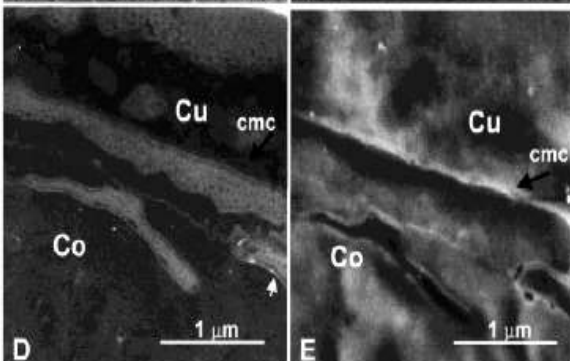
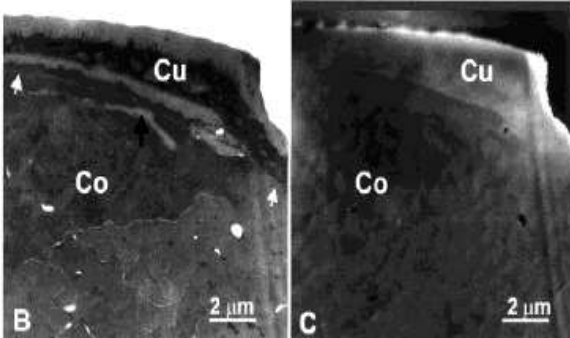
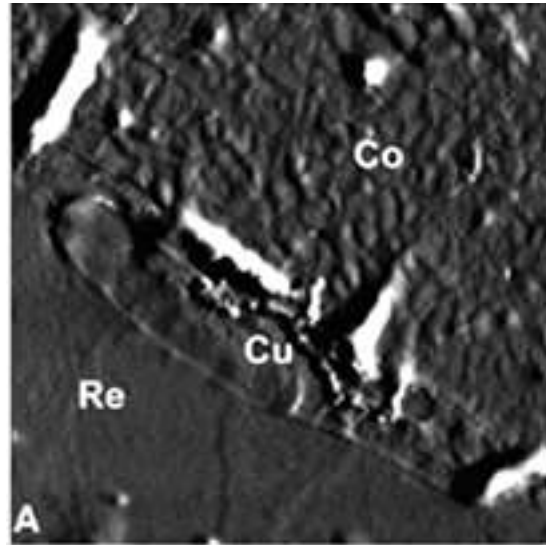
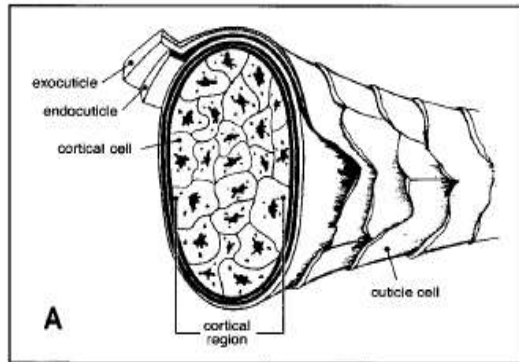
•Relevant to Muscular Disease Diagnostics and monitoring



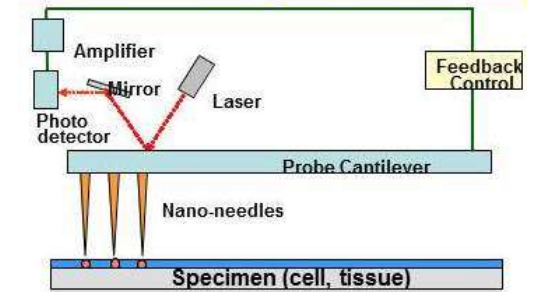
Shroff et al, *Am J Physiol* 1995

# Correlative Nano-Indentation and Tissue Elasticity with an AFM

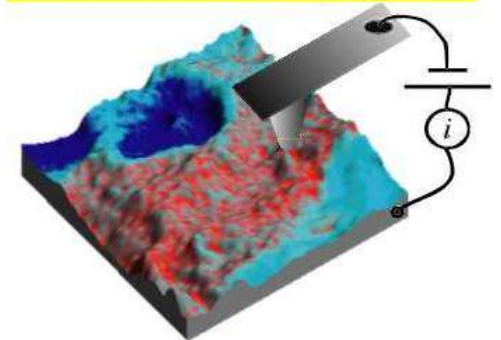
Tissue stiffness-based diagnosis (cancer, MS, ALS, osteoporosis)  
Understanding How Acupuncture works



## Nano-acupuncture



## Nano-electro-acupuncture

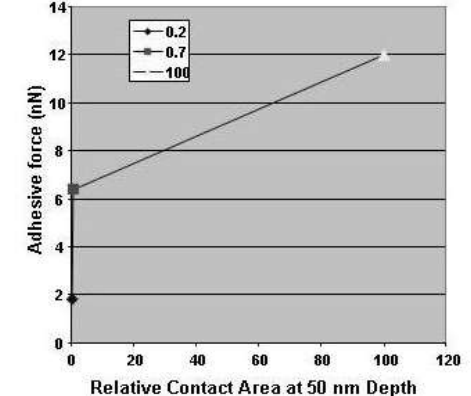
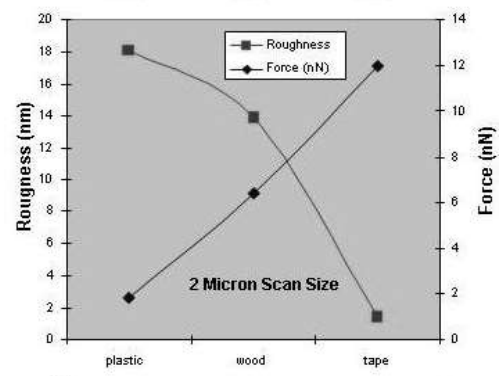
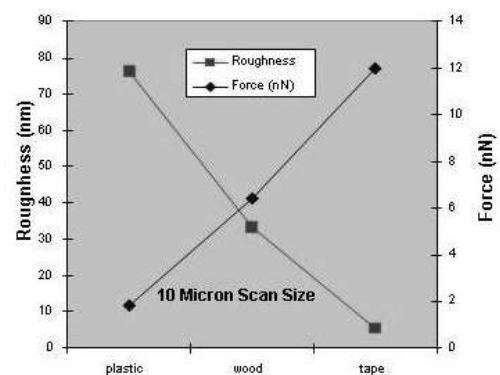
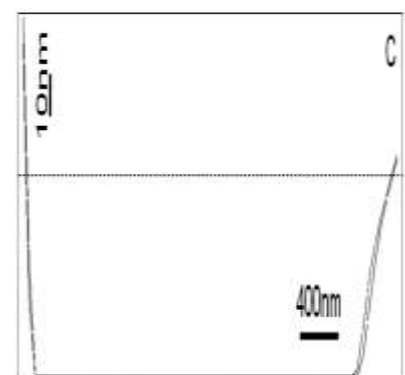
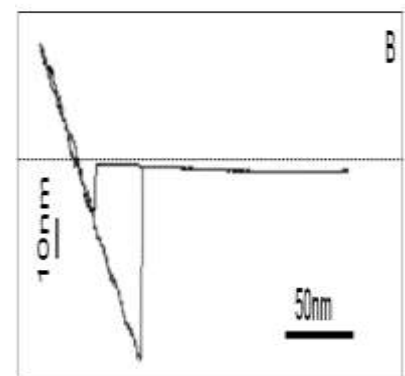
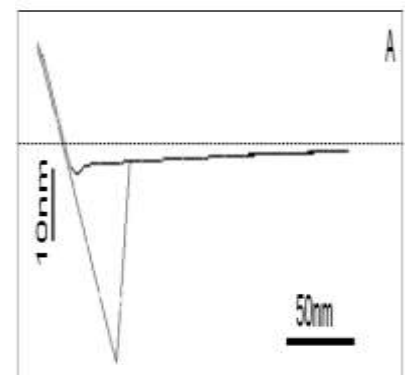
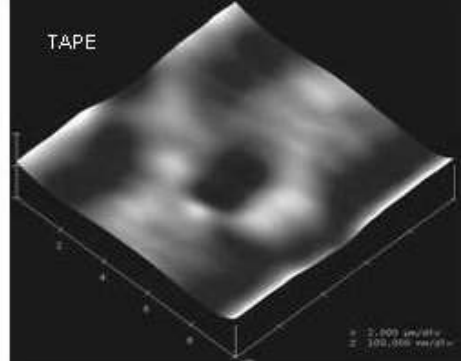
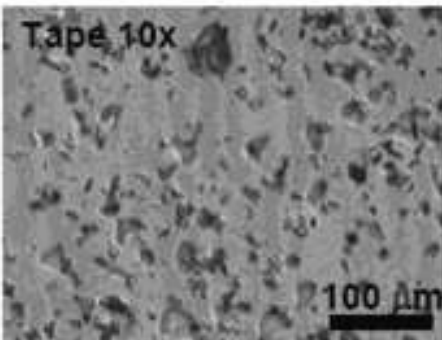
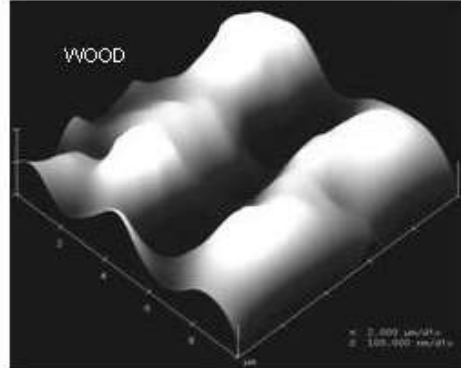
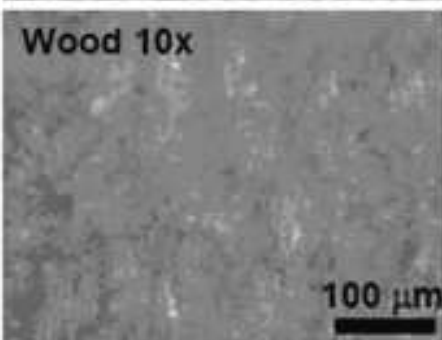
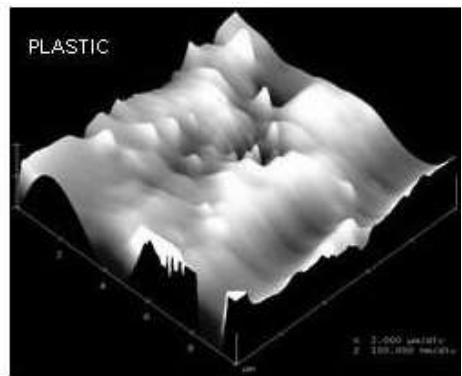
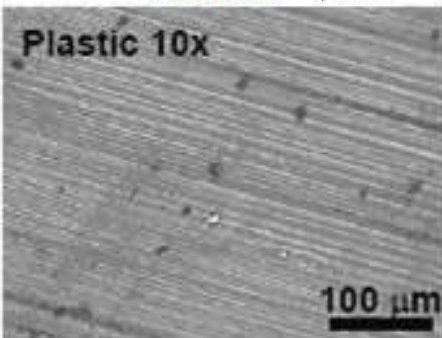
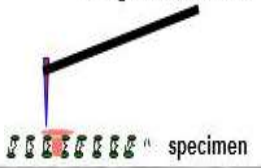




# Stickiness and Surface Roughness Of Composite Materials

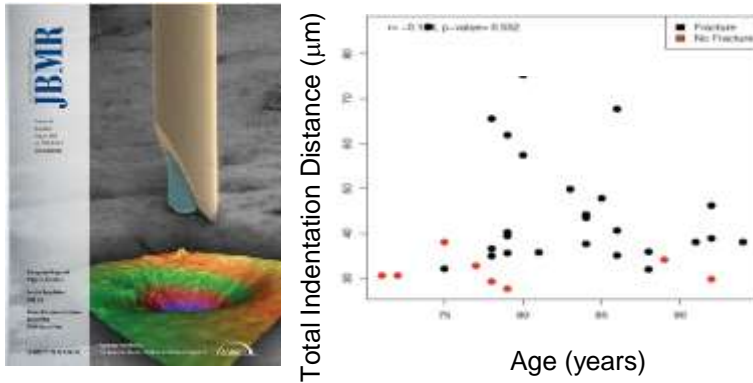
Diagnostics for Infectious bacterial biofilm, sepsis, cell-substrate adhesion

Integrated cantilever



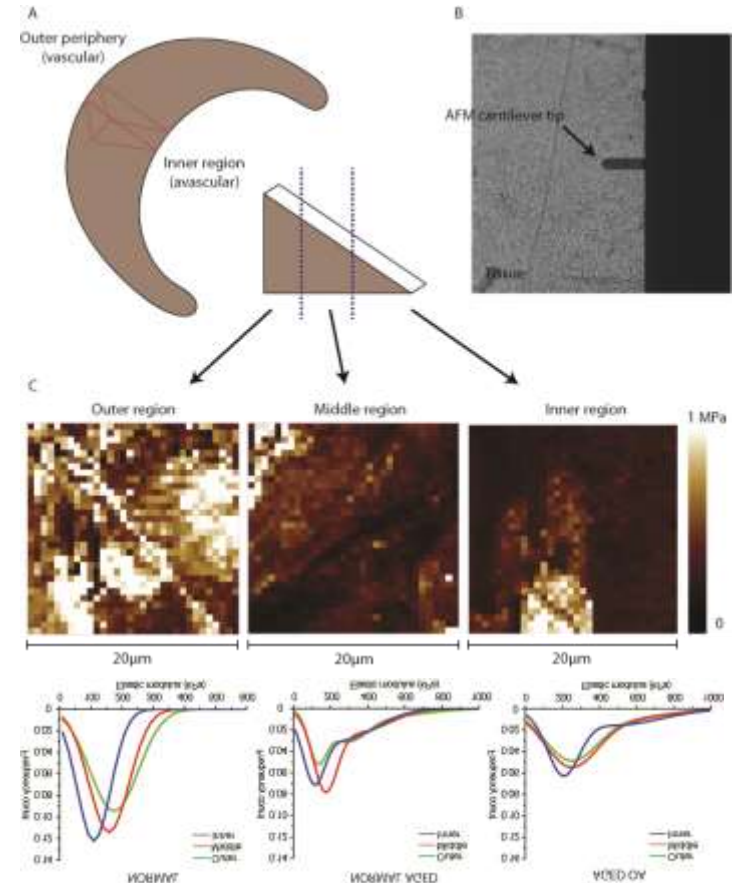
# Diagnosing/Treating human diseases

## Patients with fractures: Indentation diagnosis



A Perez, R Güerri, X Nogues, E Cáceres, MJ Peña, L Mellibovsky, C Randall, D Bridges, JC. Weaver, D Brimer, KJ. Koester, RO. Ritchie, PK. Hansma, JBM, 25, 1877-85 (2010)

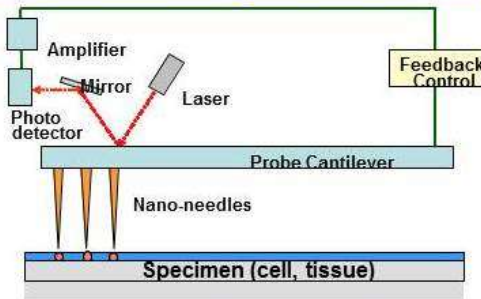
## nanomechanics of human menisci



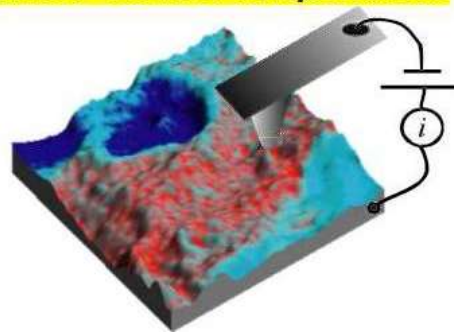
Kwok et al.

Nanomedicine: Nanotechnology, biology, Medicine, in press, 2014

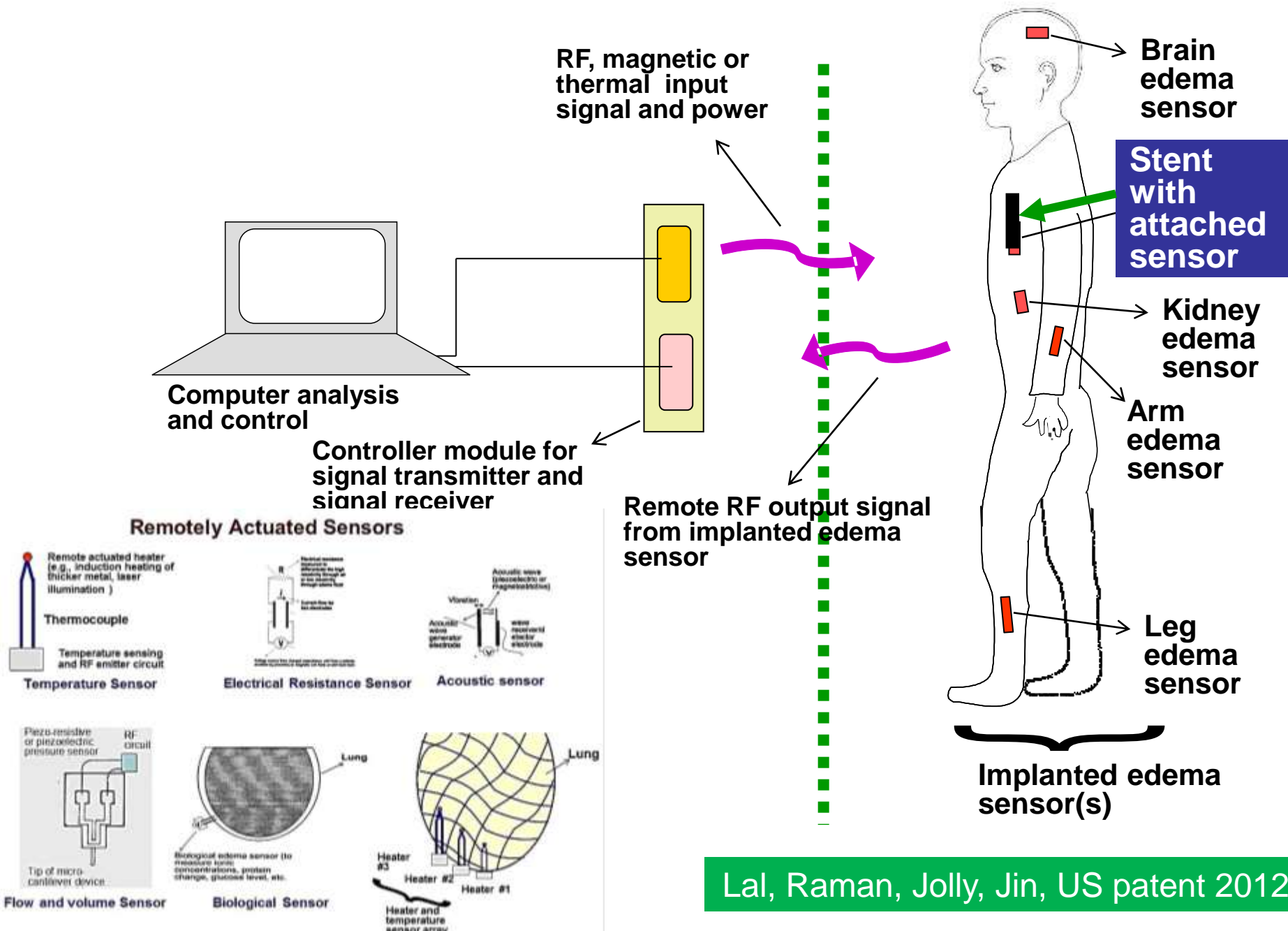
## Nano-acupuncture



## Nano-electro-acupuncture

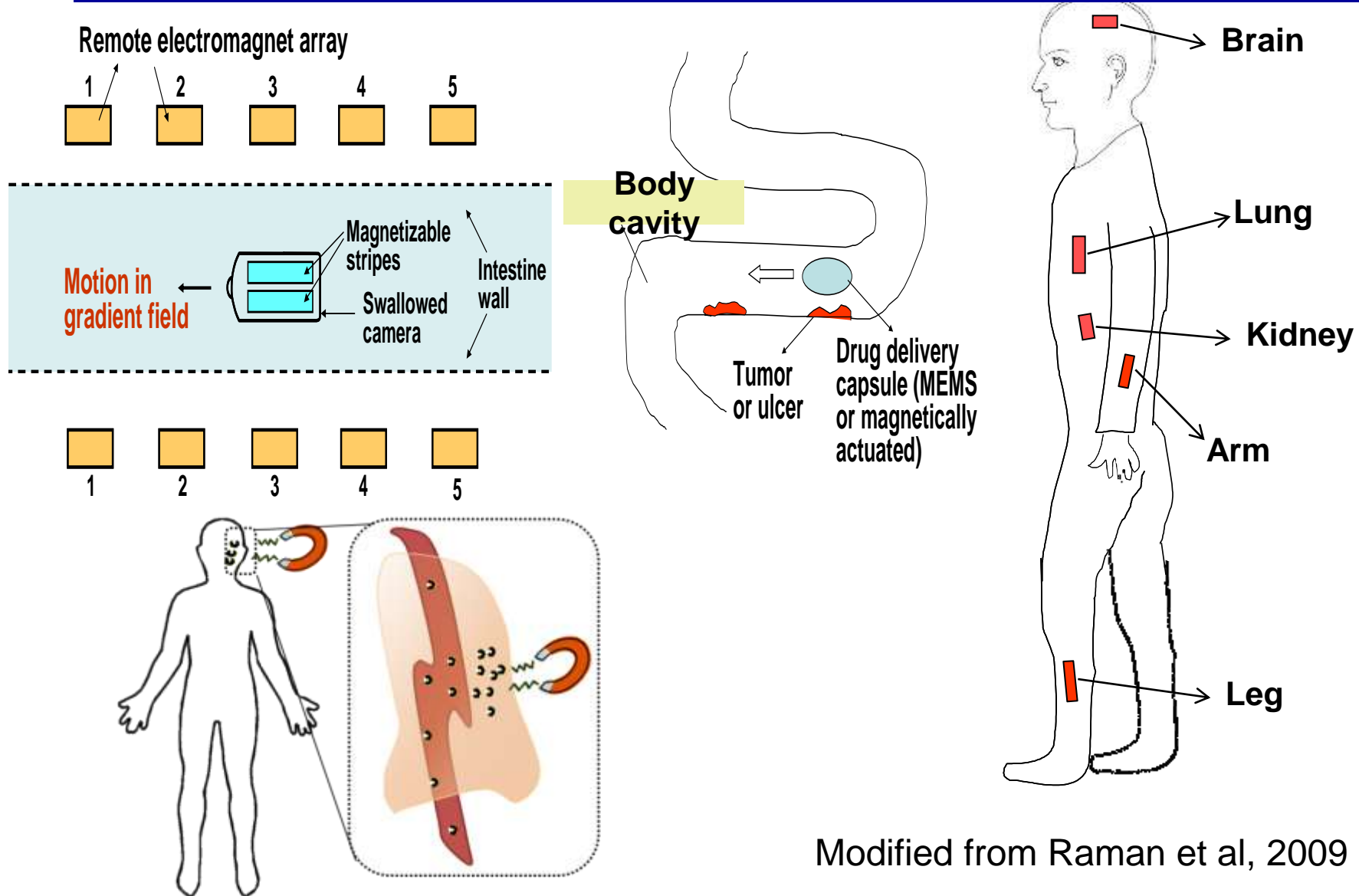


# Remote Sensor System for Various Organs/Tissues



# Remotely Guided in-vivo Theranostics

## Nanodelivery for Diagnosis and Therapy



- Nanotubes
- Nanoclusters
- Nanoshells
- Dendrimers
- **Nanoliposomes**
- **Magnetically-vectored Nano-capsules**
- **Nano bowls, nano-golf balls**

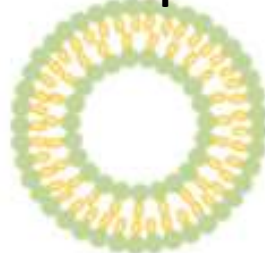
### Therapeutic Carriers



Polymeric NPs



Micelle



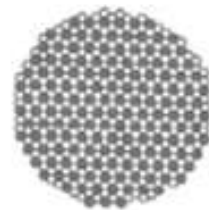
Liposome



Nanogel



Dendrimer



Silica NP

### Diagnostic Augments



Magnetic NP

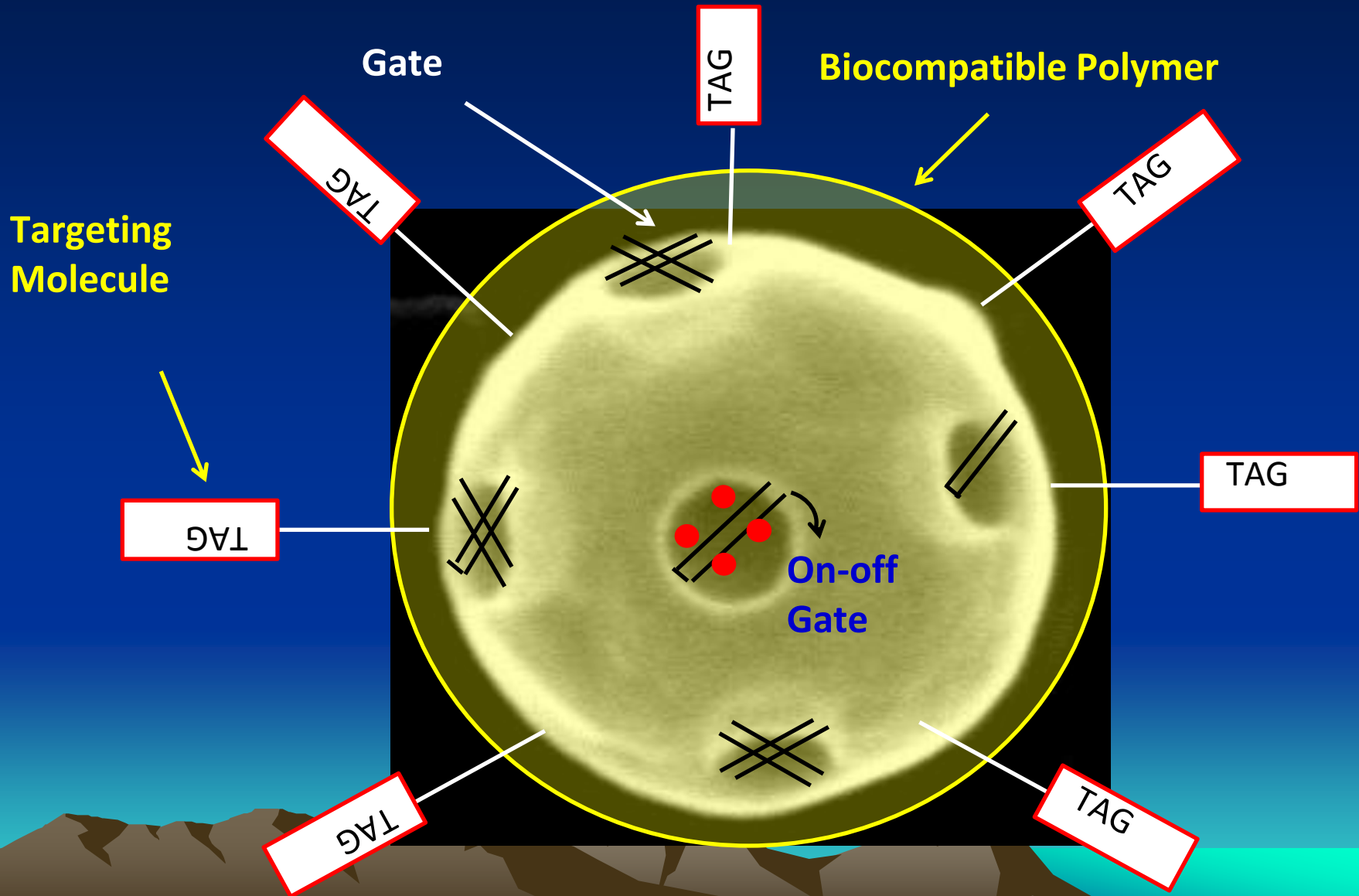


Gold NP



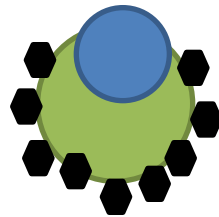
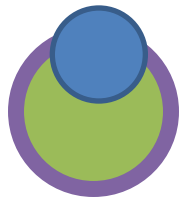
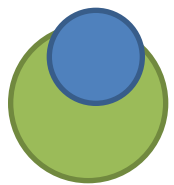
Quantum dot

# Controlled and Targeted Theranostic NanoCapsules

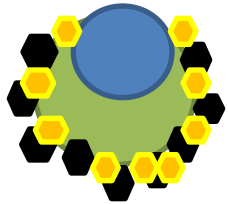


# Magnetic Gold/Silica Nano Bowls and Capsules

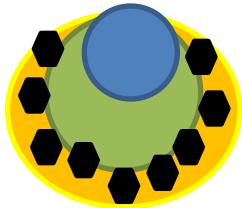
**For Targeting and controlled delivery**



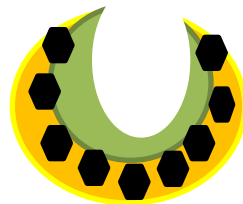
Silica Olive bowl Amine Functionalize Iron Oxide particles



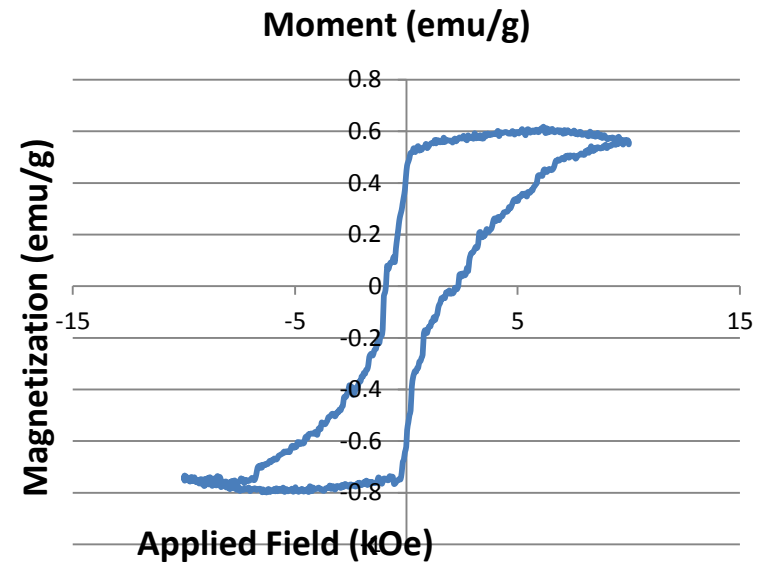
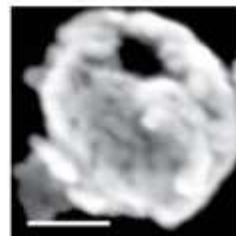
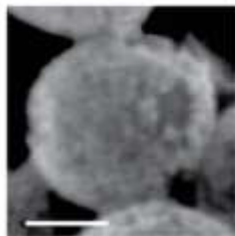
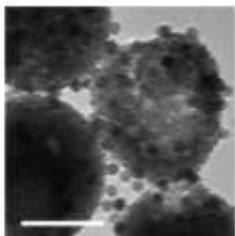
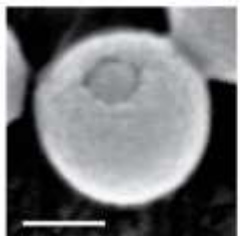
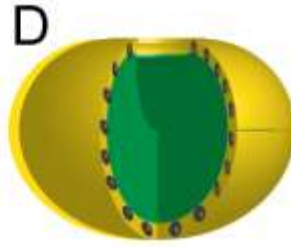
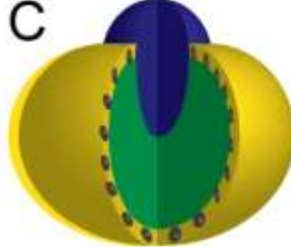
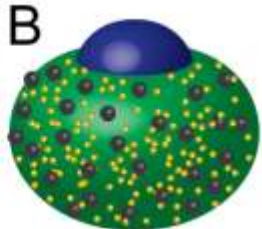
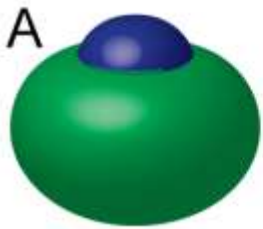
Gold Seed



Gold Plate

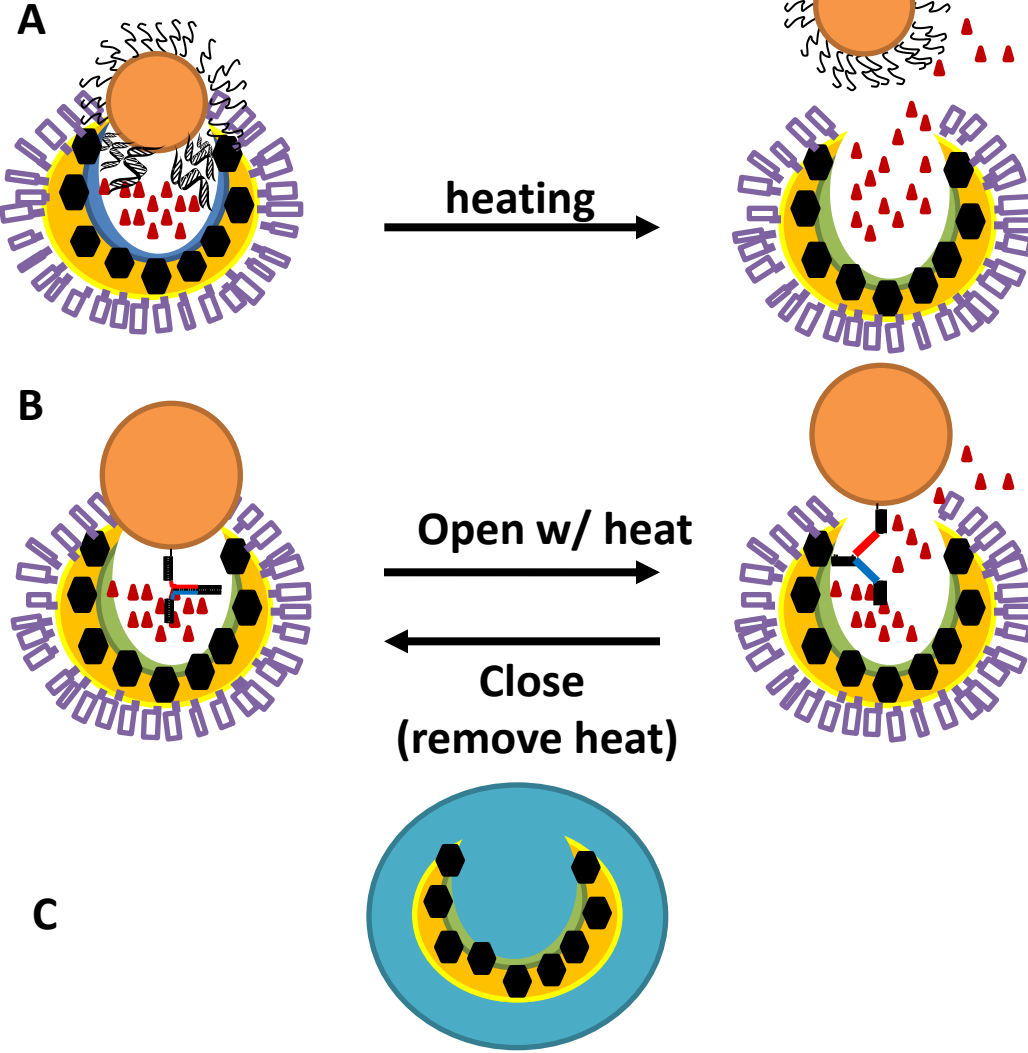


Remove PS core

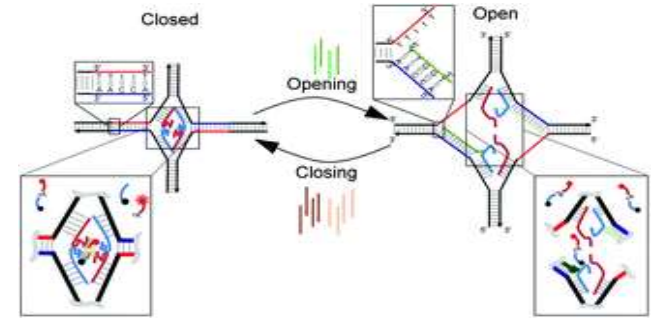


Under patent embargo

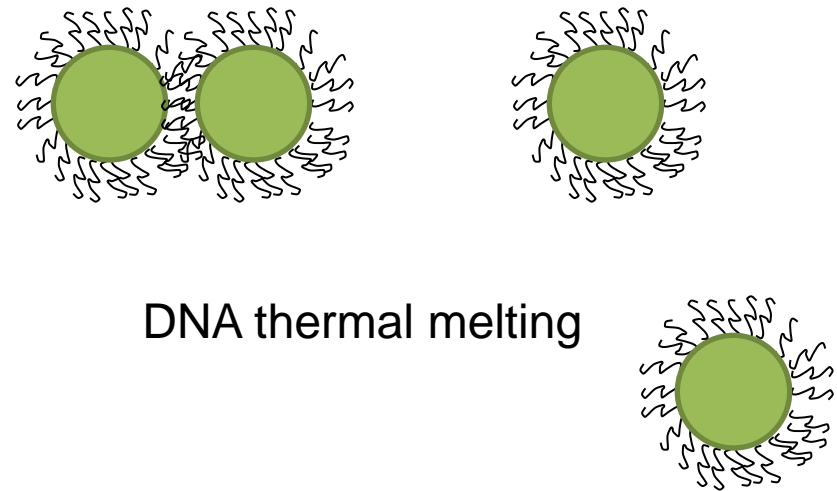
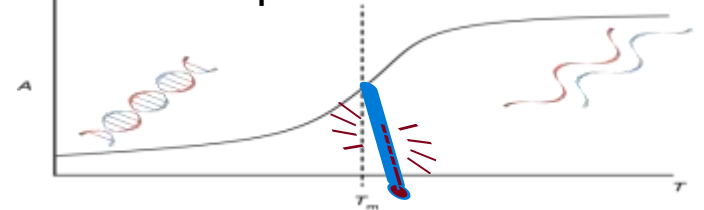
# Controlled Release using stimuli-sensitive Caps/coating



## DNA based conjugation and actuation



## Strand Displacement Devices



DNA thermal melting

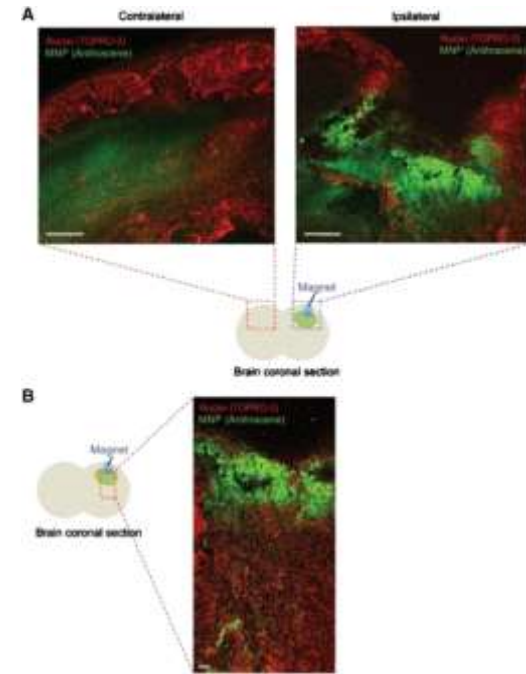
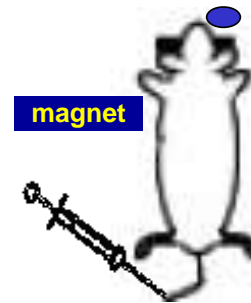
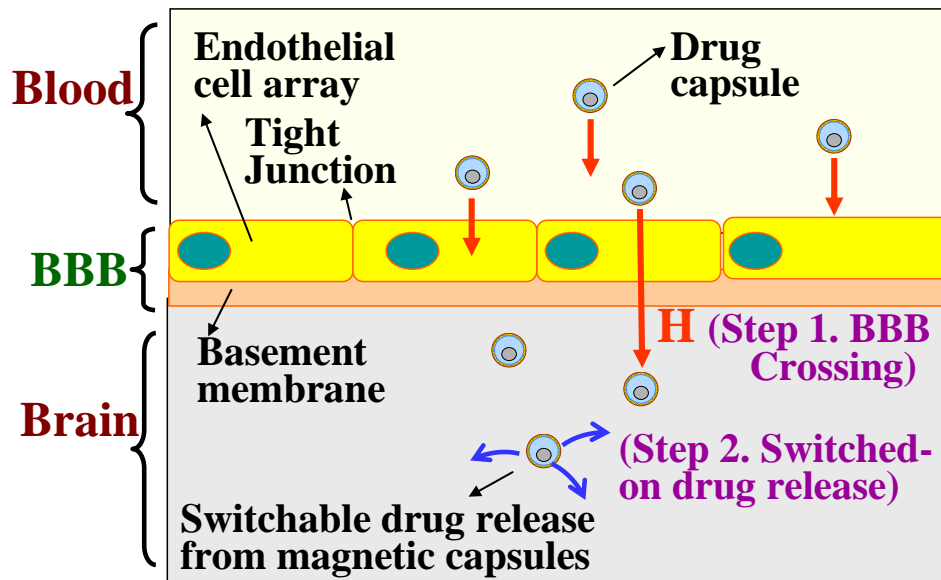
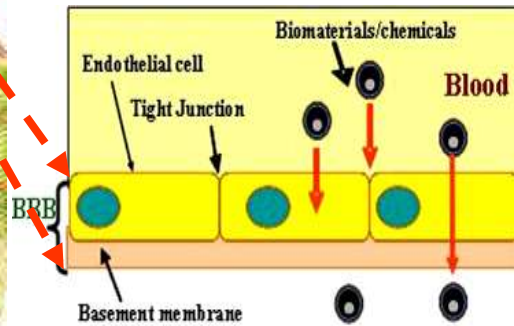
Under patent embargo

**A:** DNA closing  
**B:** DNA motors opening and closing  
**C:** encapsulation in hydrogel.



# For Brain Diagnosis and Therapy

## BBB crossing by gradient magnetic field



Permanent or electromagnet



# Nano-Bio Lab

## Interdisciplinary Team

**Nanobiophysicists**  
**Nanotechnologists**  
**Material**  
**Scientists/Engineers**  
**Biochemists**  
**Cell and system Biologists**  
**Medical Doctors**

## **Funding:**

**NIH**  
**NSF**  
**RC Nano Corp**  
**Alzheimer's Assoc**  
**Cal Dept of Health**

## **Group Members:**

### **Research Scientists:**

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**Fernando Arce Ph.D.**

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**Brian Meckes**

**Jeanie Kwok**

**Michael Hwang**

**Joon Lee**

**Nirav Patel**

**Mukunth Vaidyanathan**

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**Nader Bagherzadeh**

**Sinduja Karl Marx**

**Alan Gomez**

**Suri Sherman**

**Celine Liong**

**Max Yang**

**Pavan Kanekal**

**Sanam Mozaffari**

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**Tissue engineering/biomaterials**

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**Veronica Shubayev, MD**

**Neurosurgery**

**Michael Karin, PhD**

**Biochemistry and Molecular Biology**

**Farooq Azam, Ph.D.**

**Scripps Oceanography Institute**

**Ashok Deniz, PhD**

**Scripps Institute**

**Brian Eliceri, PhD**

**Cell Biologist**

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**RC Nano Corp**

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**Neeraj Jolly, M.D.,**

**Cardiologist, U Chicago**