Scanning Probe Microscopy for Medical Applications

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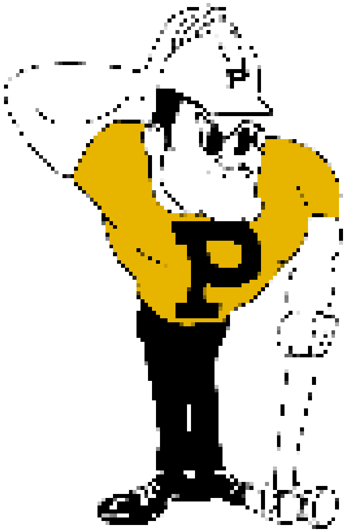

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Outline

Basics of Scanning Probe Microscopy

SPM Integration and Optimization for Medical Applications

- Neuroscience and other applications
- Force Microscopy – Modified Lateral
- Hyperbaric AFM Development
- Magnetic and Electric Force Microscopy

Summary with Discussion

QUESTIONS?

Scanning Probe Microscopy (SPM)

- •Scanning Tunneling Microscopy – Rohrer and Binnig 1982
- •Atomic Force Microscopy (AFM/SFM) – Binnig et al 1986

Resolution:

Optical – 200nm

AFM – atomic resolution ***possible***

– tip dimension, detection system, operating conditions & controls

Measurement Capabilities:

Topography ***and***

Material Characteristics

mechanical

electrical

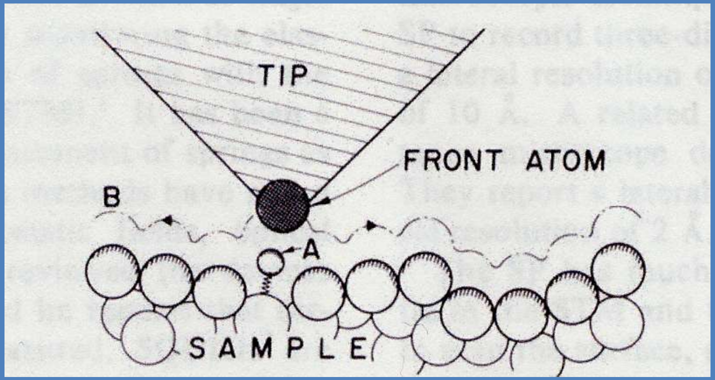
chemical…..

Operating Conditions:

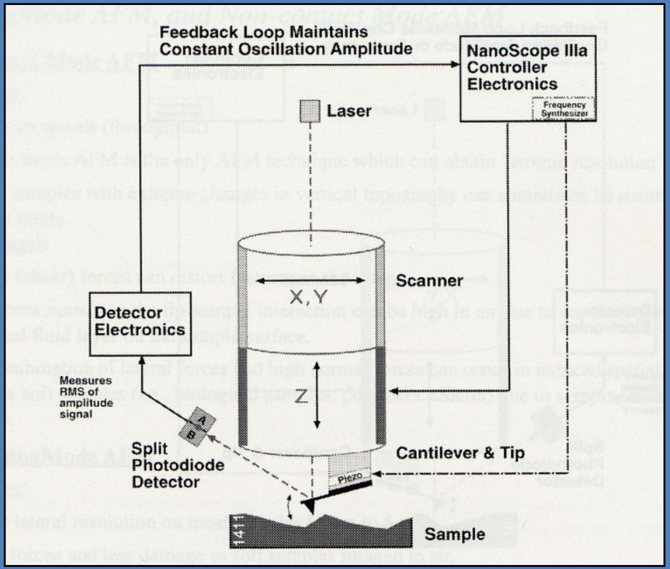
Vacuum, air (gas), liquid,

and now in hyperbaric conditions

D'Agostino, D.*, McNally, H.A., & Dean, J.B., (2012). Hyperbaric atomic force microscopy. Journal of Microscopy, 246, (2), 129-142.



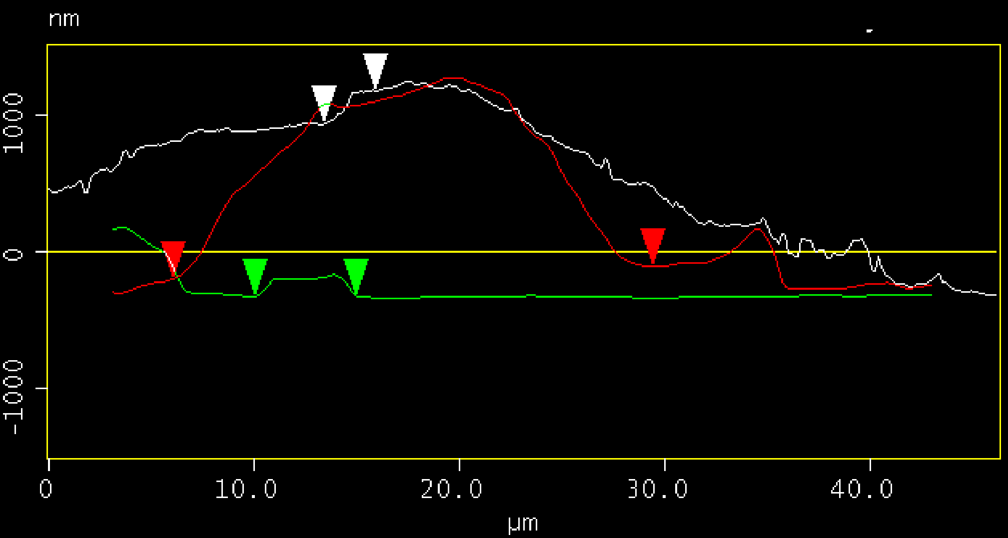
Principle of Operation,
Binnig, G., Quate, C.F., & Gerber, Ch., Atomic Force Microscopy, Physics Review Letts, 1986, Vol. 56, No. 9, pp. 930-933.



Bruker, Dimension 3100, BNC 1039

Other Established Types of Scanning Probe Microscopy

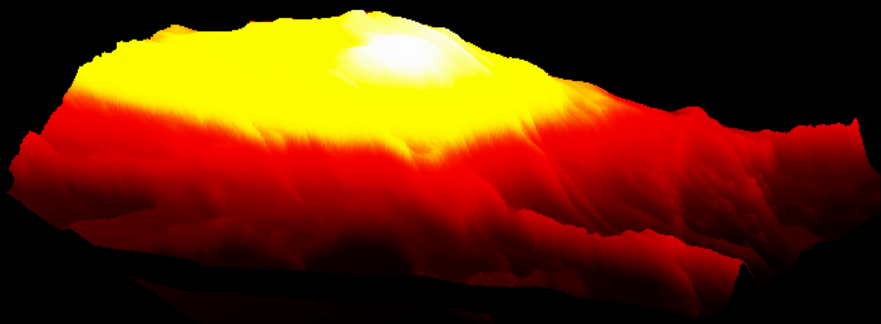
CFM, chemical force microscopy
C-AFM, conductive atomic force microscopy
ECSTM electrochemical scanning tunneling microscope
EFM, electrostatic force microscopy
FMM, force modulation microscopy
FOSPM, feature-oriented scanning probe microscopy
KPFM, kelvin probe force microscopy
MFM, magnetic force microscopy
MRFM, magnetic resonance force microscopy
NSOM, near-field scanning optical microscopy (or SNOM, scanning near-field optical microscopy)
PFM, Piezoresponse Force Microscopy
SCM, scanning capacitance microscopy
SECM, scanning electrochemical microscopy
SHPM, scanning Hall probe microscopy
SICM, scanning ion-conductance microscopy
SPSM spin polarized scanning tunneling microscopy
SSM, scanning SQUID microscopy
SSRM, scanning spreading resistance microscopy
SThM, scanning thermal microscopy
STP, scanning tunneling potentiometry
SVM, scanning voltage microscopy

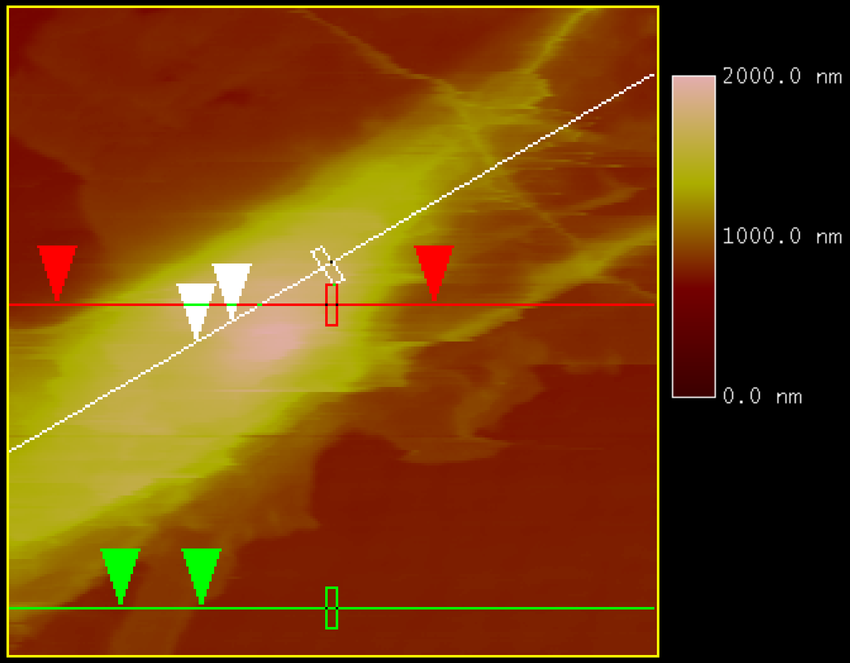


Cell Body Parameters

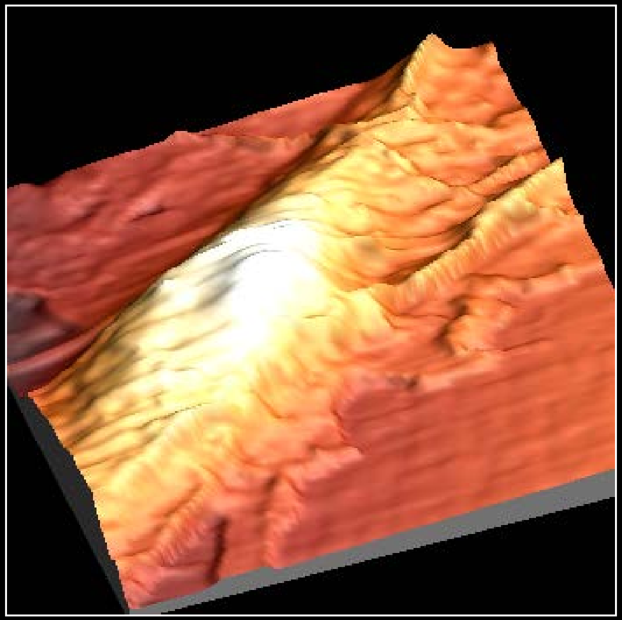
10X20 µm in diameter

1-4µm high





Height Mode Image



3-D Reconstruction

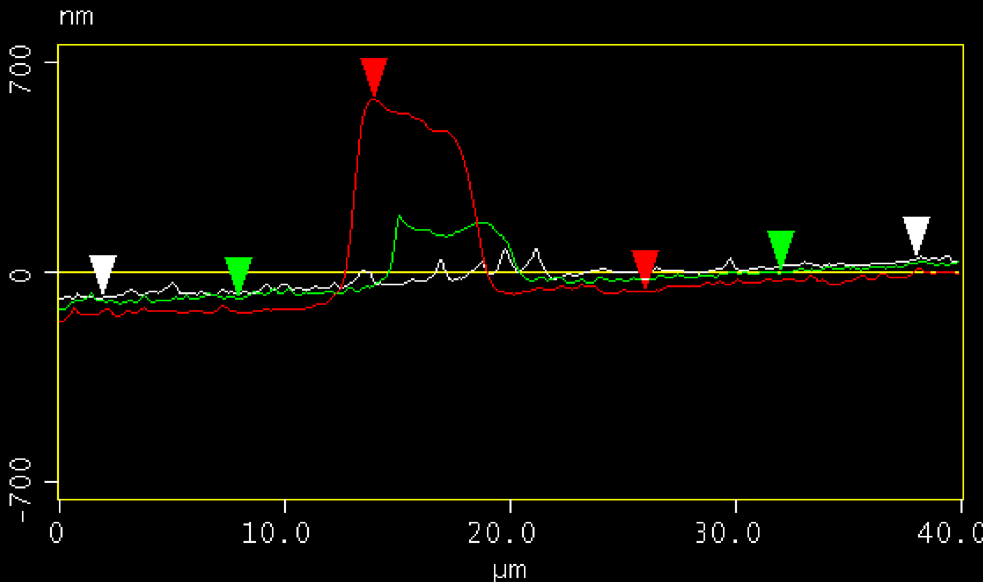
H.McNally and R.Borgens, Journal of Neurocytology, V.33, I.2, (2004) pp. 251-258.

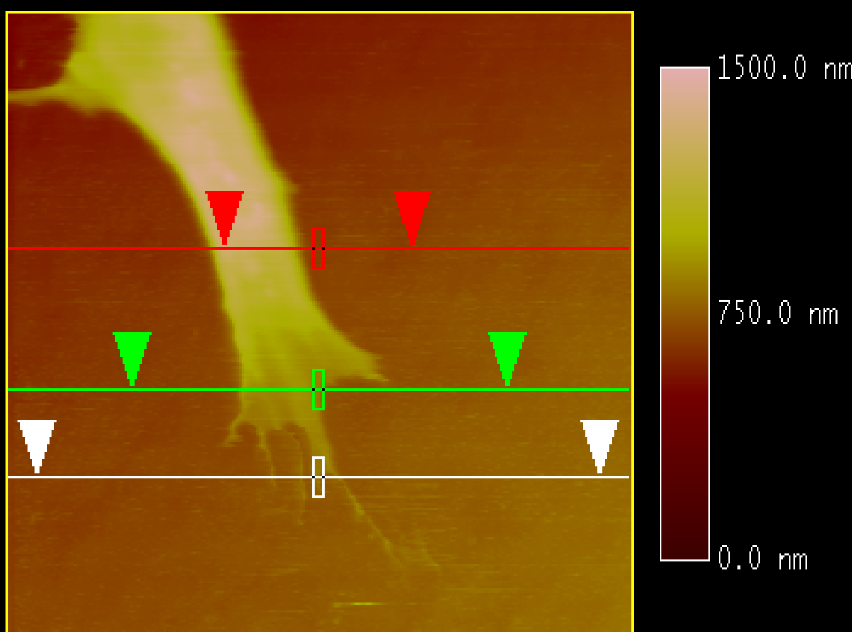
Growing Process Parameters

Neurite: 6.03 ± 2.1 µm wide and 385.1 ± 192.7 nm high with vertical projections of 94.87 ± 70.2nm, n=15

Growth Cone: 10.3 ± 2.89 µm wide and 260.4 ± 176 nm high with vertical projections averaging 258.5 ± 148.6 nm, n=15

Axonal Spines: ranged in caliber from 100nm to 1µm and 1 – 2 µm in length, n=5



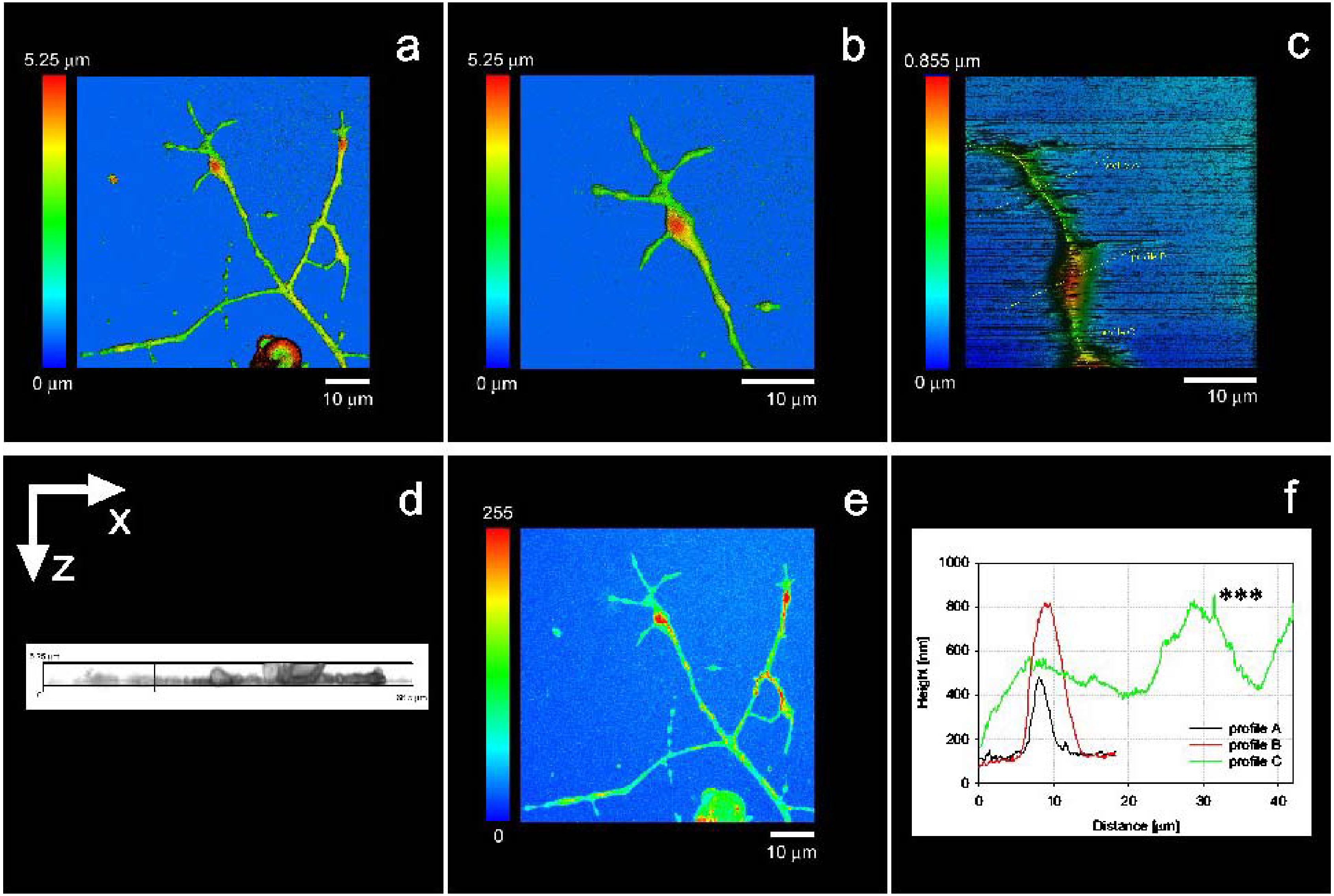


Height Mode Image

3-D Reconstruction

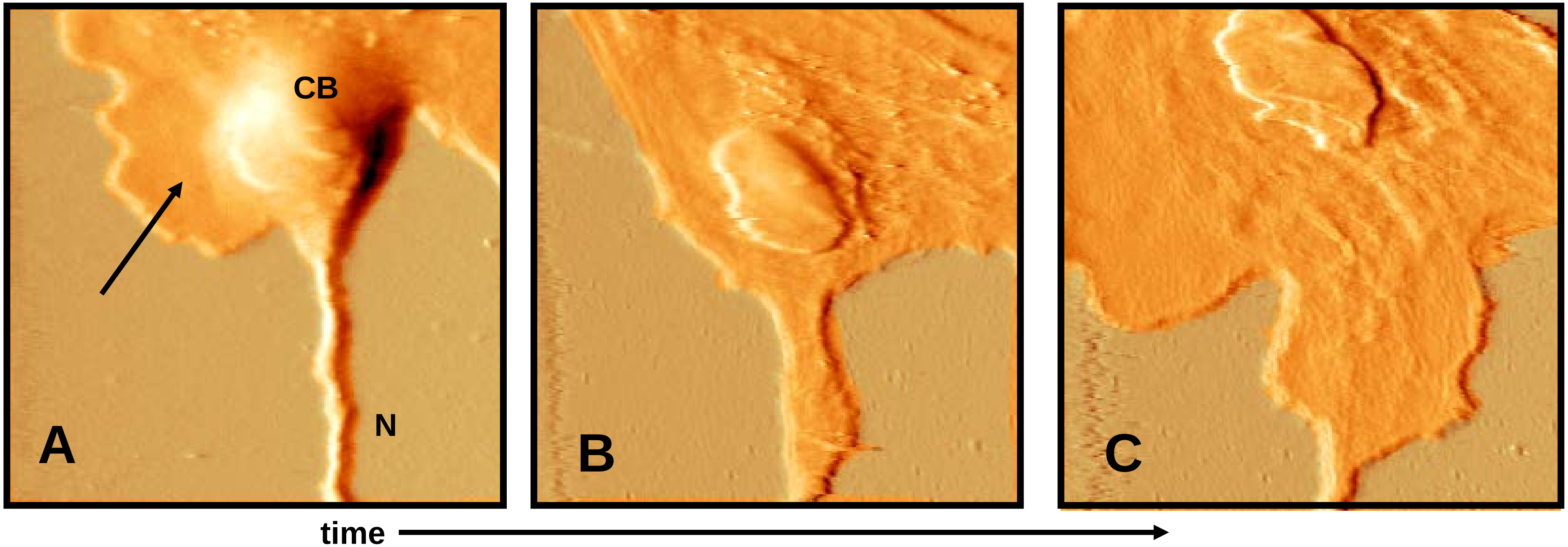
H.McNally and R.Borgens, Journal of Neurocytology, V.33, I.2, (2004) pp. 251-258.

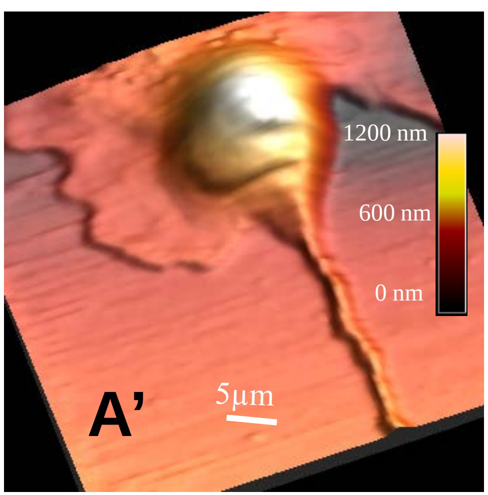
AFM Compared to Confocal Microscopy

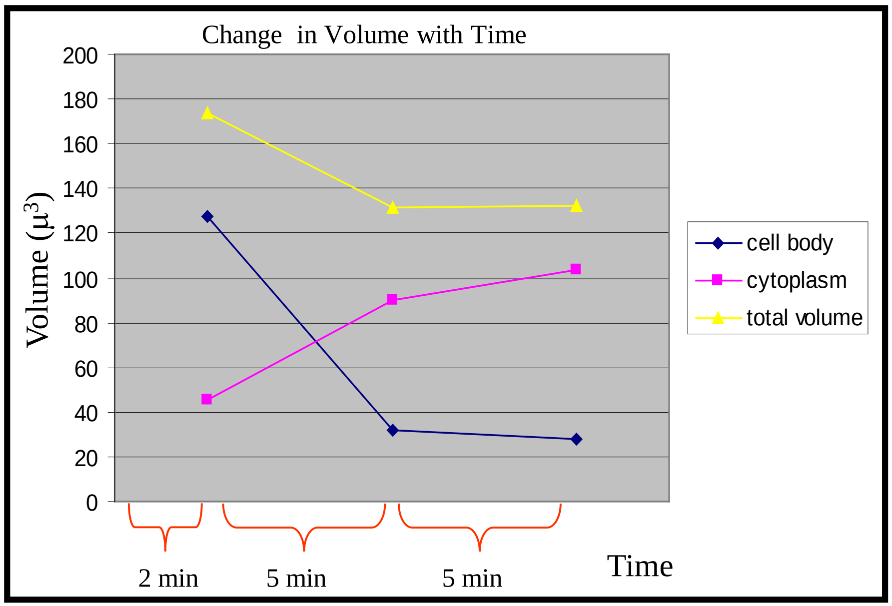


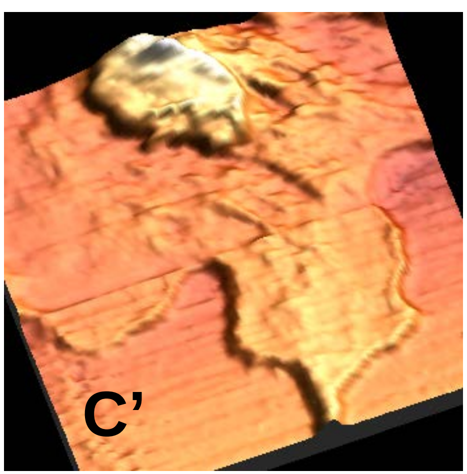
H.McNally, B. Rajwa, J. Sturgis, and J.P. Robinson, "Living Neuron Morphology Imaged with Atomic Force Microscopy and Confocal Microscopy" Journal of Neuroscience Methods, V. 142 (2005) pp.177-184.

Cell Death by AFM Probe

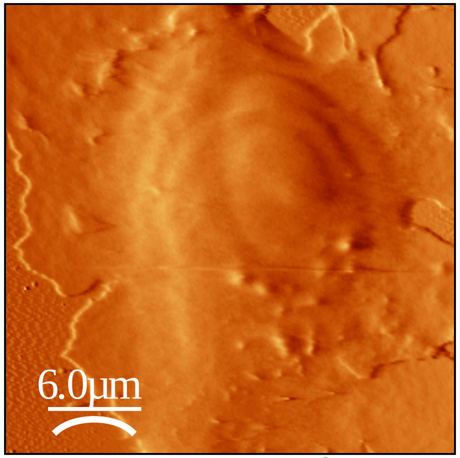




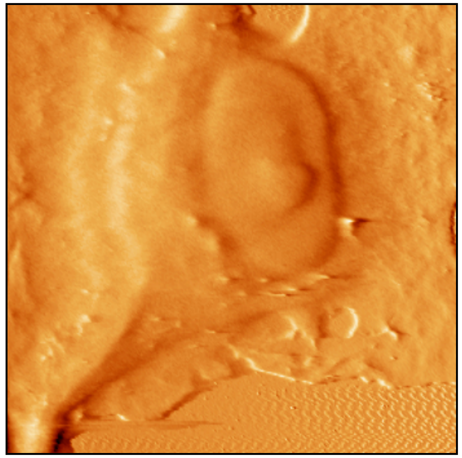




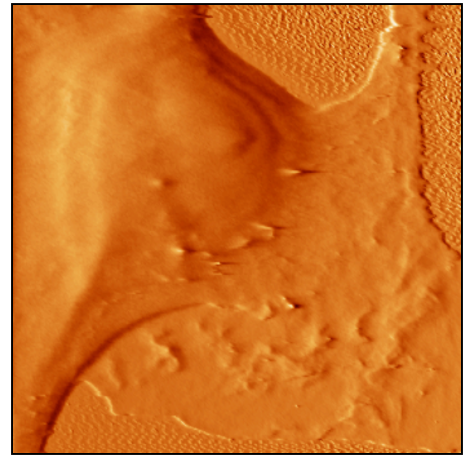
Effects of Endotoxin - Acrolein



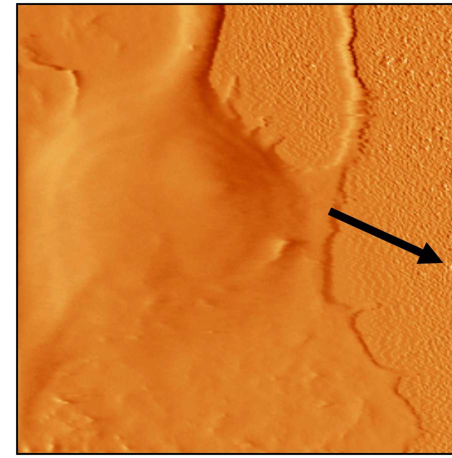
Prior to acrolein



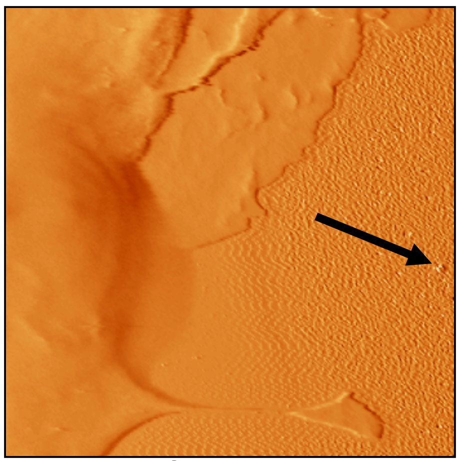
T+15min



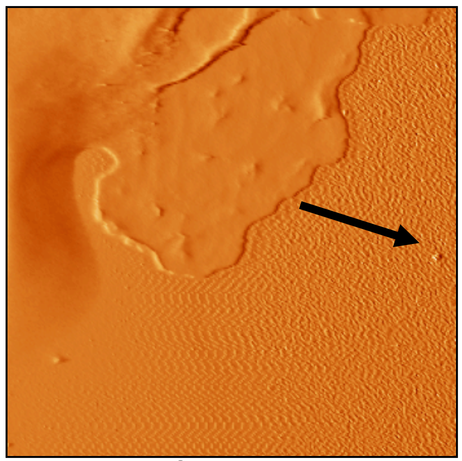
T+35min



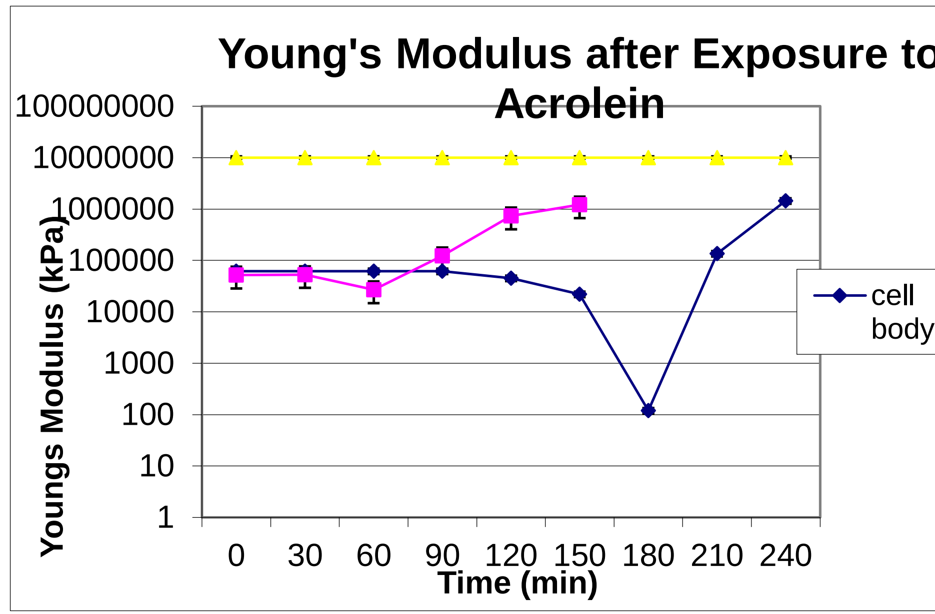
T+55min



T+1hr,15min

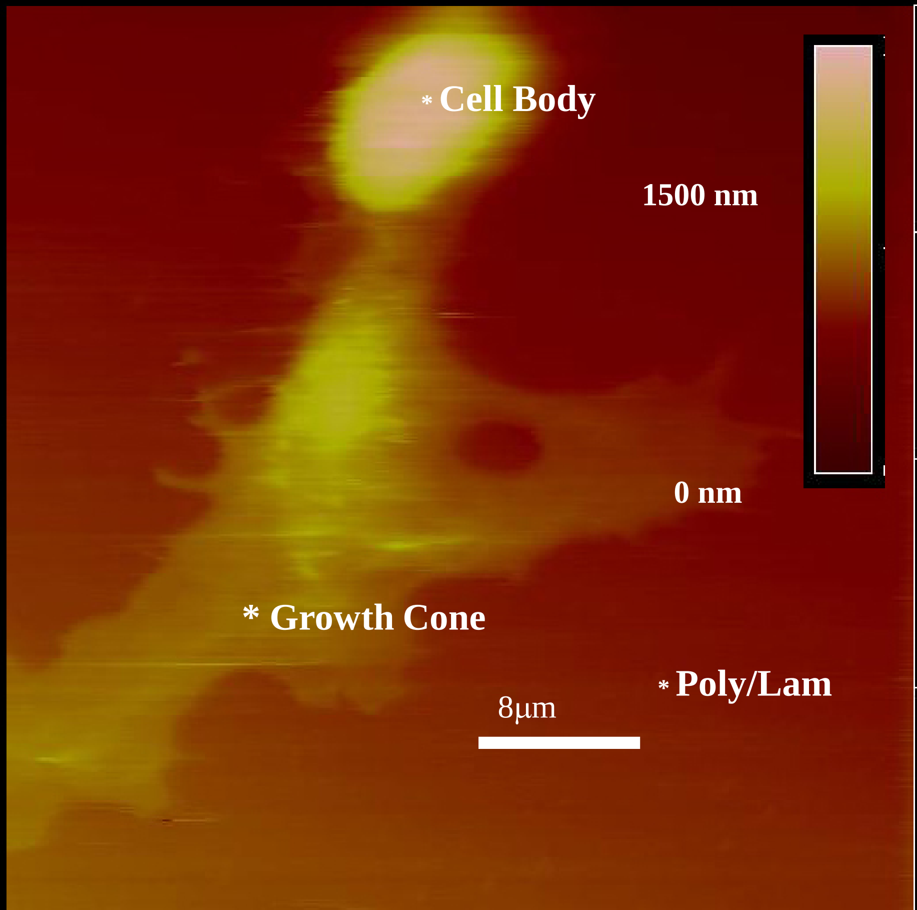


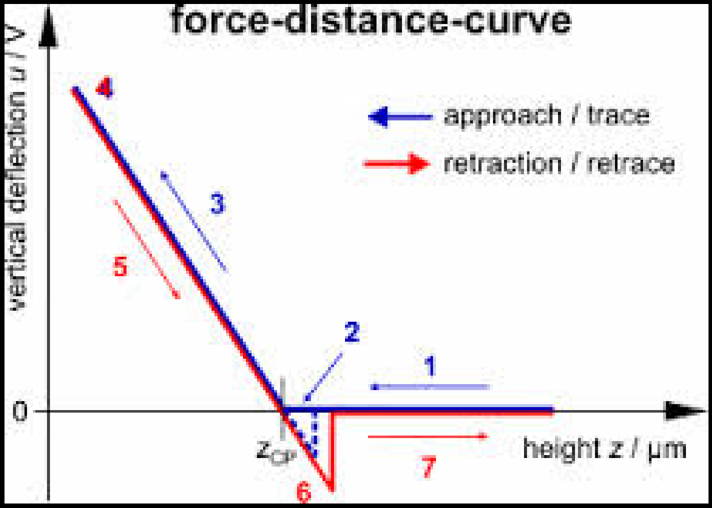
T+1hr,25min

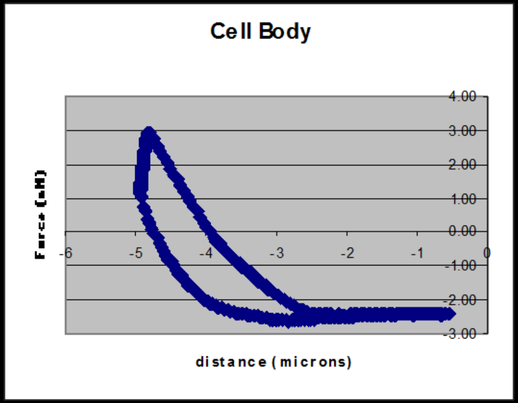


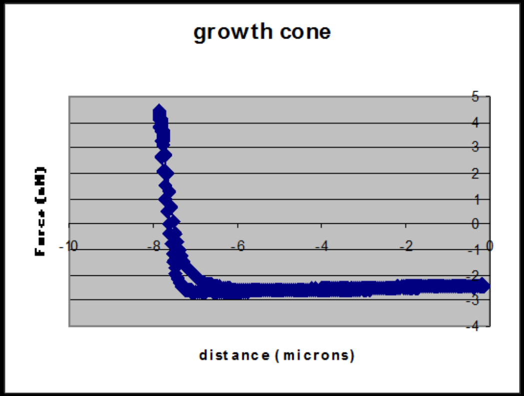
P. Liu-Snyder, H. McNally, R. Shi, R. Borgens, "Acrolein-Mediated Mechanisms of Neuronal Death", Journal of Neuroscience Research, V.84, pp.209-218, (2006)

Force Measurements – Membrane Elasticity









Average Elasticity

Cell Body: 60KPa

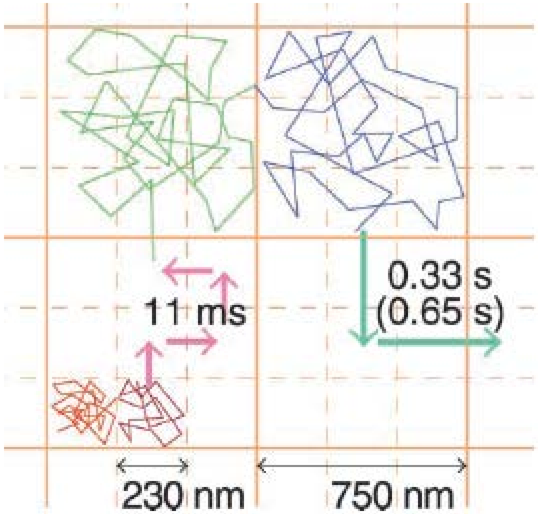
Growth Cone: unknown

M. Mustata, K. Ritchie, H. McNally, Journal of Neuroscience Methods, V. 186, pp.35-41 , January 2010

Probing Cellular Membrane Structure and Elasticity with Atomic Force Microscope

Mirela Mustata, Helen McNally, Ken Ritchie

The goal of this project is to probe the cellular membrane and underling cytoskeleton using AFM to understand the mechanical properties of the cell and especially the structure of the ultrafine compartments of cytoskeleton underlining the cellular membrane. Previous research on neurons show that the composition and biochemical properties of the cytoskeleton differ in the neuron cell body from the properties of the cytoskeleton associated with the axon.

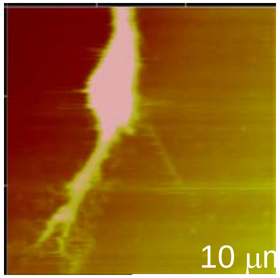


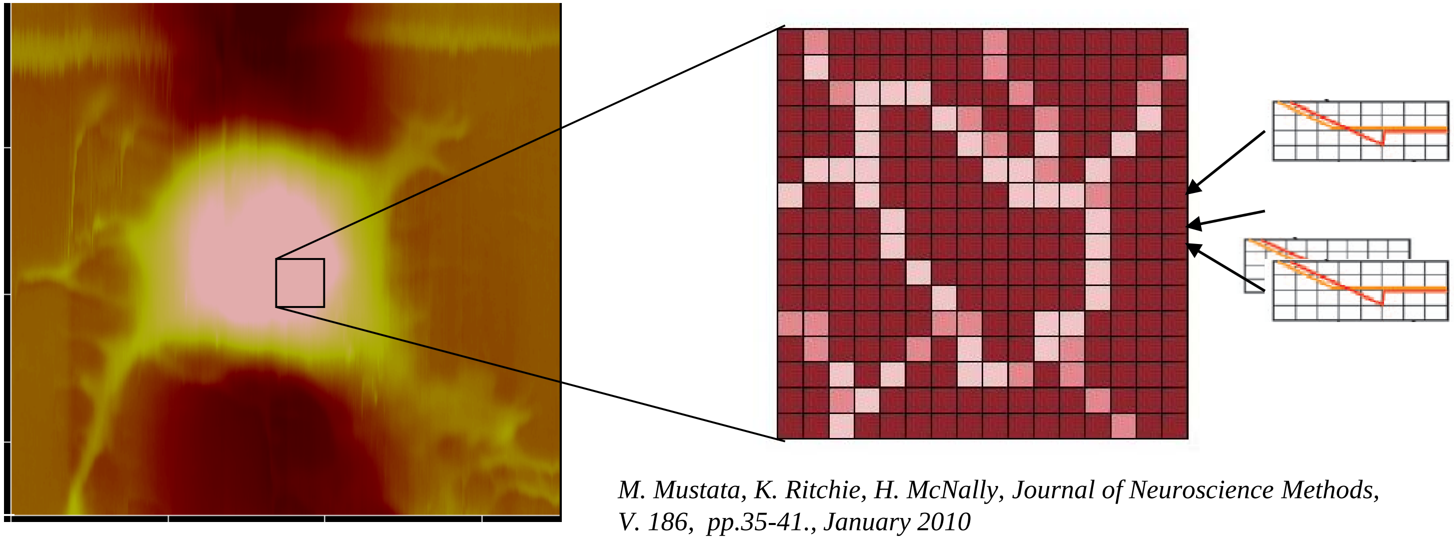
SINGLE PARTICLE TRACKING

double compartments in NRK cells.
(DOPE) undergoes diffusion inside a 230 nm compartment for 11 ms and then hops to an adjacent compartment. In the 750 nm compartments the residence time is much larger (of about 330 ms)

Fujiwara, et al. (2002) Journal of Cell Biology, 157, No. 6, 1071-1081

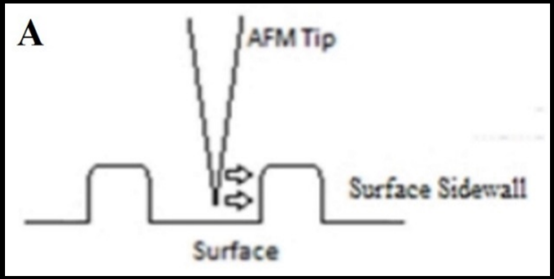
Force Volume of a 16X16 pixel surface (simulation) each pixel representing the cantilever deflection versus Z piezo position. Brighter spots correspond to higher stiffness points (actin filaments underlining the membrane)

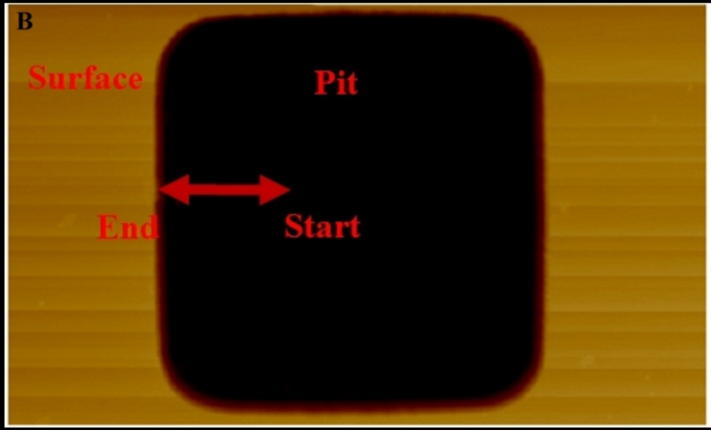


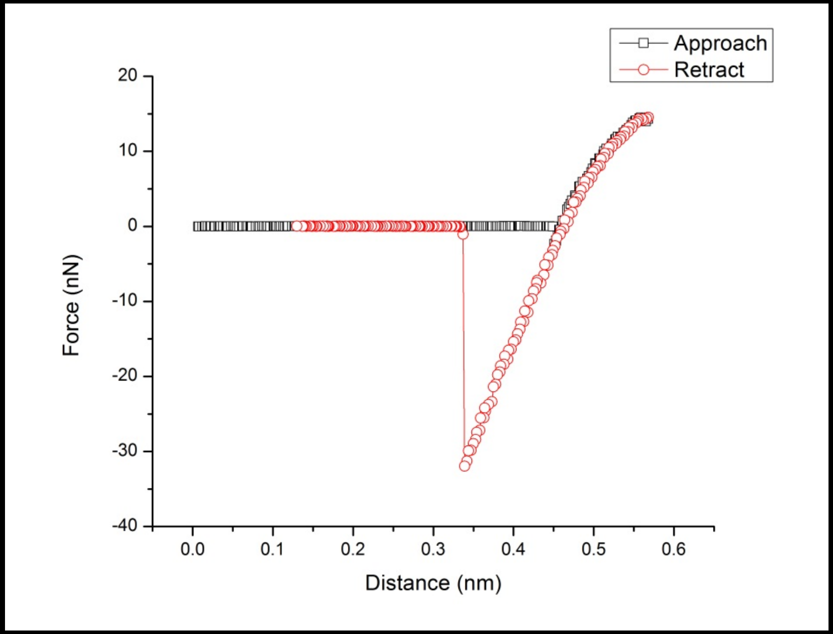


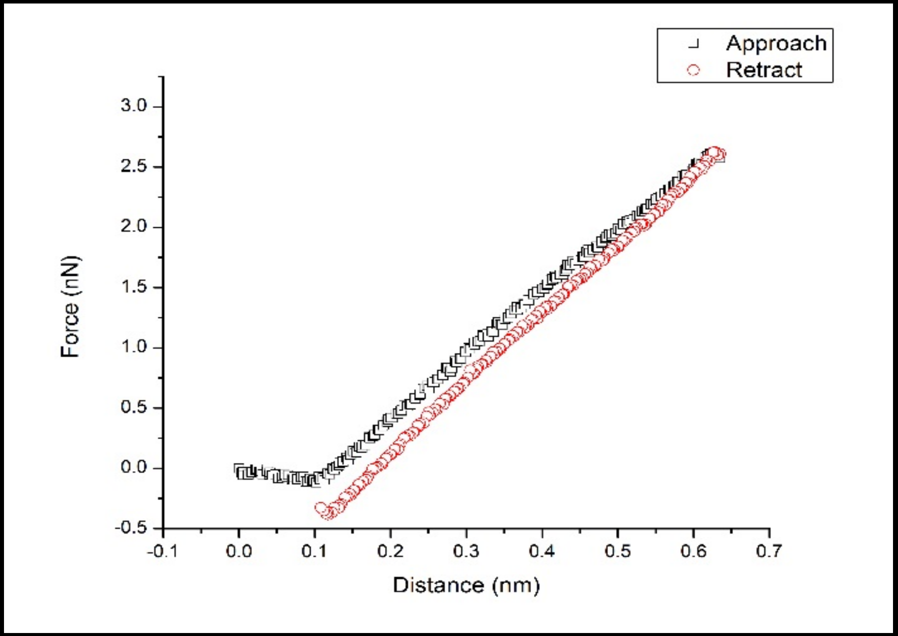
M. Mustata, K. Ritchie, H. McNally, Journal of Neuroscience Methods, V. 186, pp.35-41., January 2010

Measuring Membrane Viscosity with a Modified Lateral Force Technique



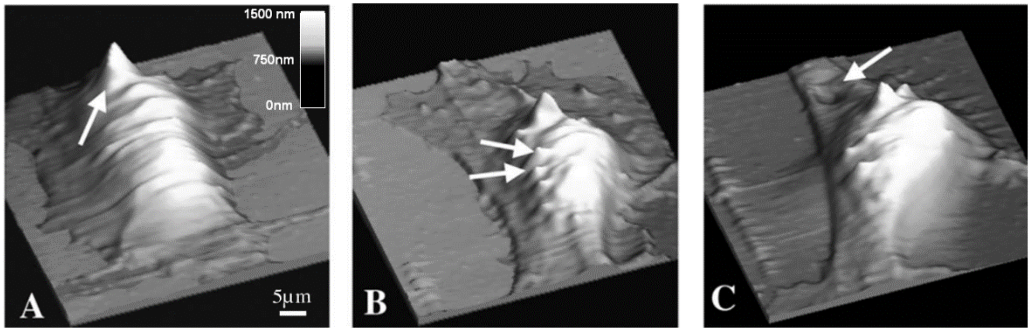






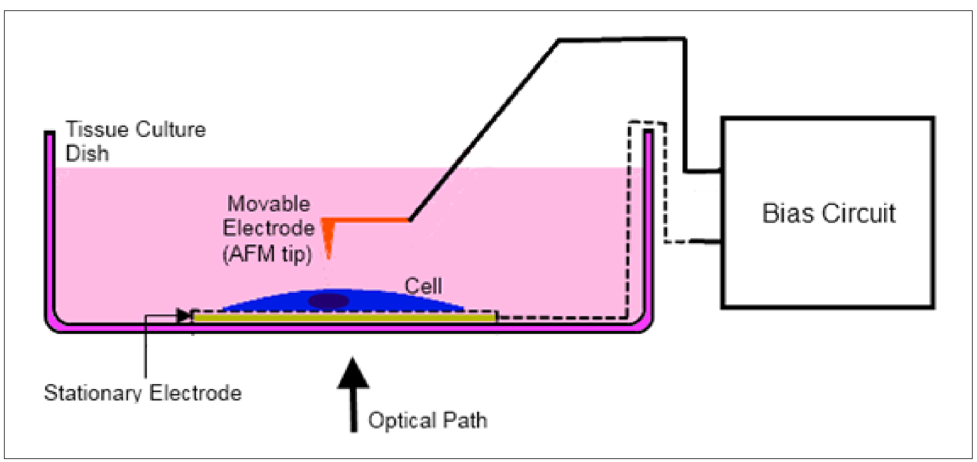
Interests in membrane changes due to disease or exposure to gas/chemicals/toxins

Vertically Directed Growth of Neurons

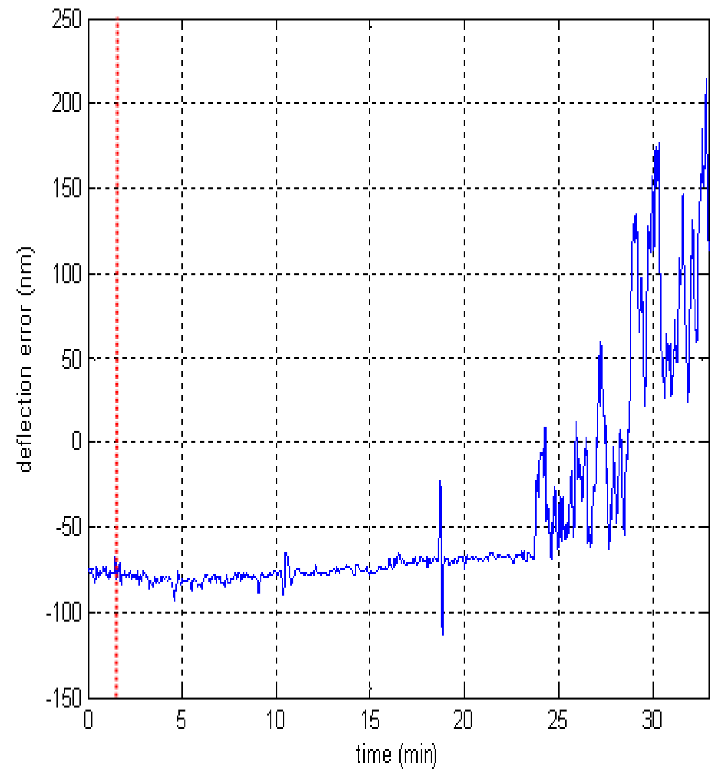


Spine like structures found in primary neurons
- growing vertically,
- appear and disappear randomly with time,
- present in cell body and growth cone

Is it possible to induce and direct the growth of z-projections?



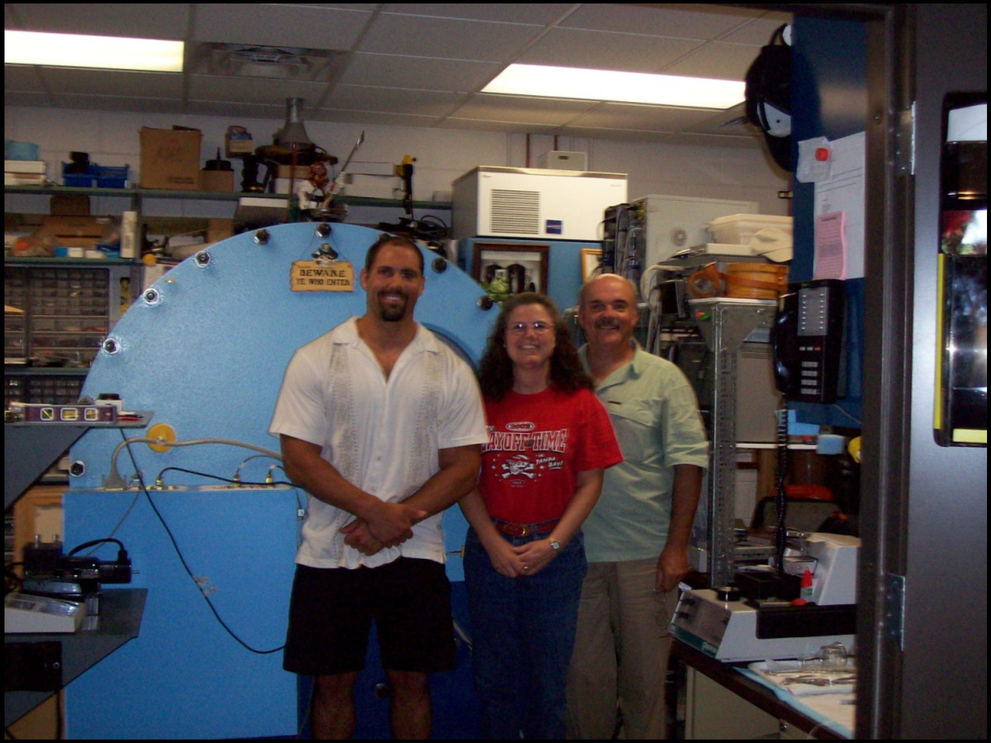
Test System 2, ITO as stationary electrode, external bias circuit applied
isolated biology and electronics,



McNally, H.A., & Abeygunasekara, W.L. An atomic force microscopy system to investigate the effects of external electric fields on neuronal Z-projections. Journal of Neuroscience Methods, in review.

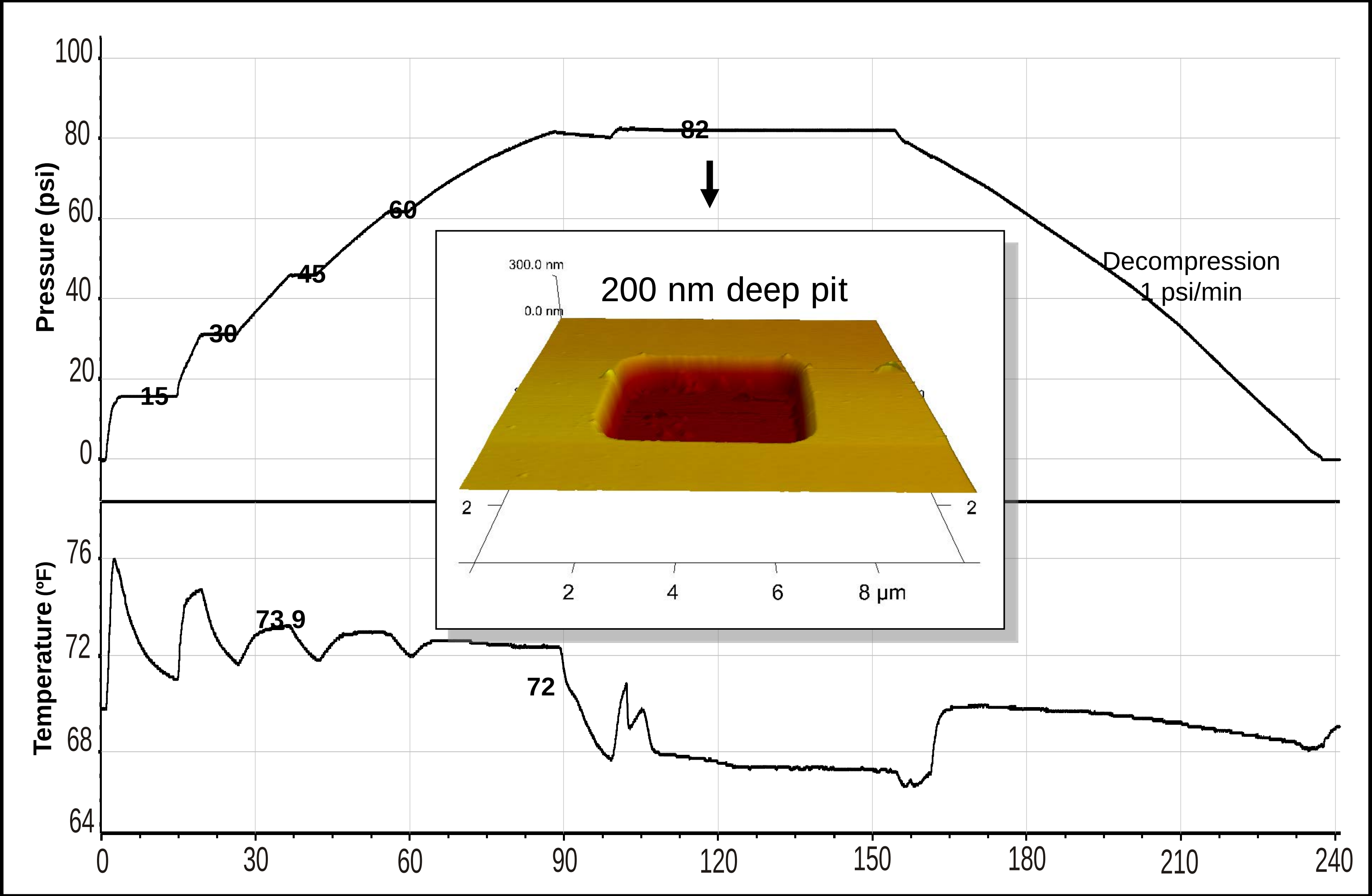
Development and testing of hyperbaric atomic force microscopy (AFM) for biological applications

Dominic D'Agostino & Jay Dean,
University of South Florida, Molecular Pharmacology and Physiology
Helen McNally Purdue University, Electrical and Computer Engineering Technology



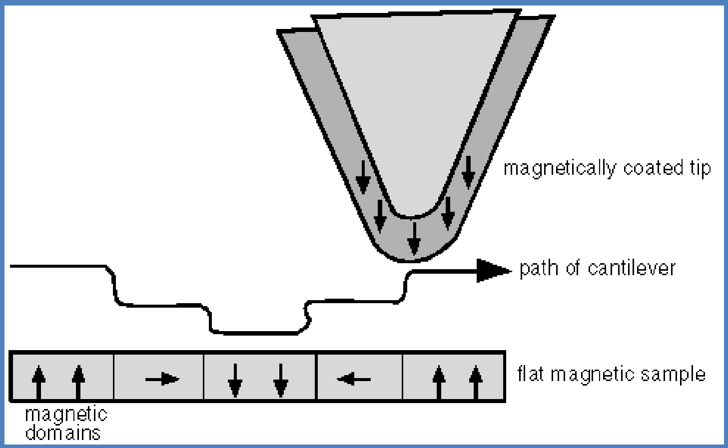
hscweb3.hsc.usf.edu/health/now/?p=96

Pressurization with Helium

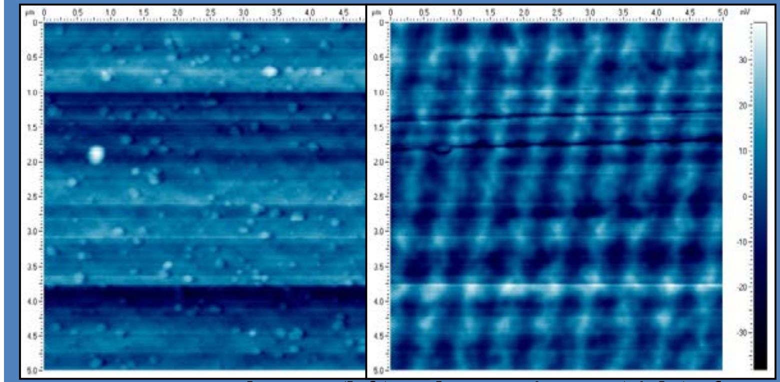


Magnetic Force Microscopy

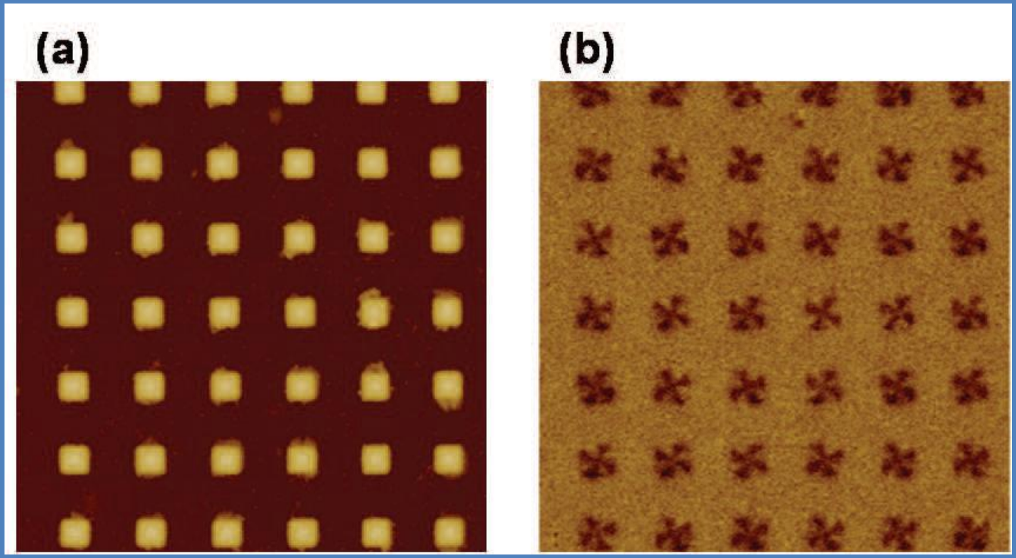
MFM images the spatial variation of magnetic forces on a sample surface.



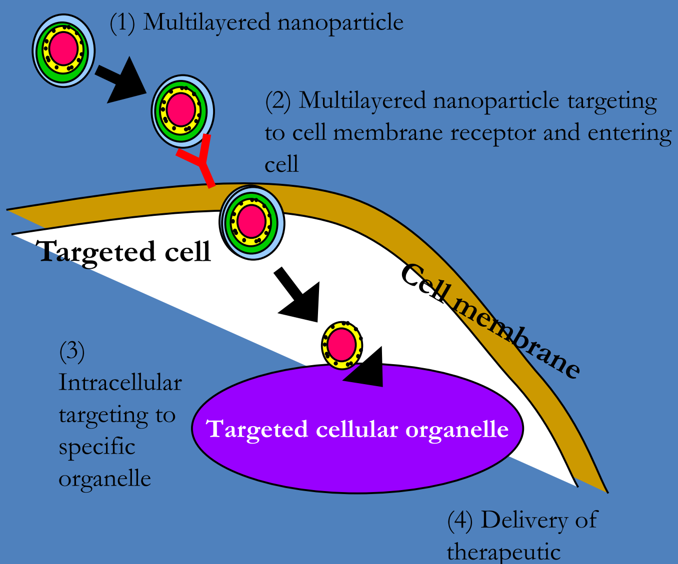
Bruker, Nanosurfaces Division



Topography scan (left) and magnetic scan (right) of magnetic tape taken with Dimension 3100.



Park Systems, (a) AFM and (b) MFM images of 2D patterned arrays of Co dot structure.



Leary and Prow, 2005

Specific Challenges to the Electro/Magnetic Force Microscopy

- Electric/Magnetic Calibration
- Resolution
- EFM/MFM in fluid
  - magnetic tips with low spring constants
  - magnetic characteristics of the solution
- External Magnetic Field required for particle magnetism
- Sensitivity (detect magnetic nanoparticles inside cells)

Additional Interest in EFM/MFM

- Technique Optimization, resolution and quantification
- Cell-to-Cell Communications
- Cell Signaling
- Neuronal magnetic aspects
- Conducting polymers, 3D scaffolding

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Yen Hseu – Osha Liang, Houston, TX

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Colleges of Technology and Engineering
Birck Nanotechnology Center

The Morton Cure Paralysis Fund
That All May Walk Again

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PURDUE UNIVERSITY
COLLEGE OF TECHNOLOGY

Thanks a Million!

QUESTIONS AND DISCUSSION

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