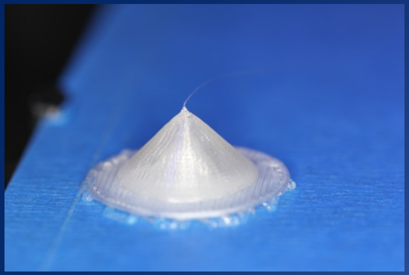


3-D Constructs--Molded vs. Printed:
The differences from a cell based perspective

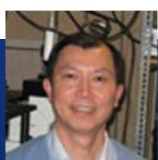
Kuan Che Fang, Miriam Rafailovich, Marcia Simon

Stony Brook University, Stony Brook, NY

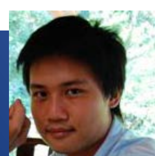
Stony Brook School of Dental Medicine

Garcia Center for Polymers at Engineered Interfaces

AT STONY BROOK UNIVERSITY

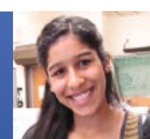


Daniel Ou-Yang



Steven Wei

Sneha Subra-manian

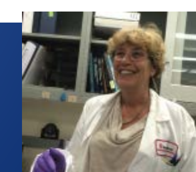


Aneri Kinariwalla

Chung-Chue (Simon) Chang

Kuan-Che Feng

Marcia Simon

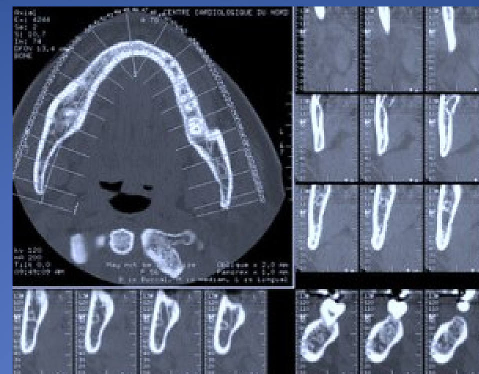


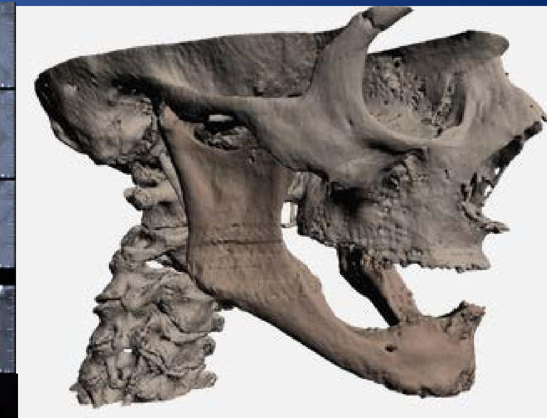
Adriana Pinkas-Sarafova

Garcia Research Scholar Program: Students from HS->Graduate work together with teachers and faculty in joint interdisciplinary research projects.

Jaw Case Study – 3D Titanium Implant (replacement)

- In 2012 an 83 year old woman with osteomyelitism – requiring jaw removal
- Patient had MRI so implant would be an anatomical match
- Jaw printed from titanium powder in a 2 day print
- Patient was eating, drinking, and speaking within 4 hours of surgery
- No FDA role





Liz Nickels, World's first patient-specific jaw implant, Metal Powder Report, Volume 67, Issue 2, March–April 2012, Pages 12-14,

Courtesy of K. Vorvolakis, FDA

This presentation does not pertain to FDA regulatory policy on Additive Manufacturing, and should not be construed as such.

Digital Additive Manufacturing – Individualizing bone augmentation

Control shape

Control resorption

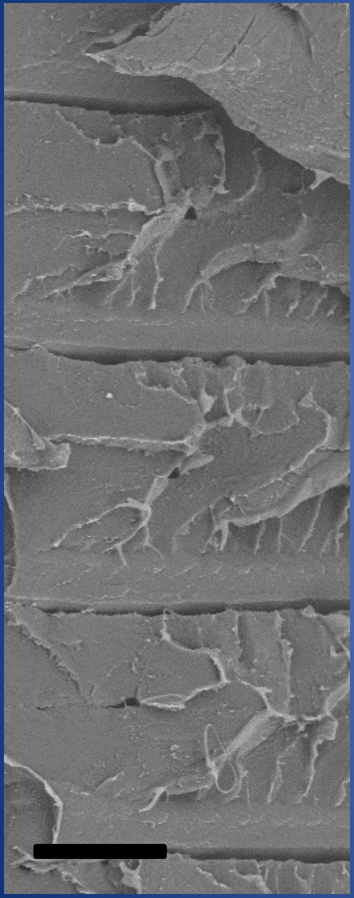
Alter materials and topography to control
- Bone formation and turnover
- Angiogenesis

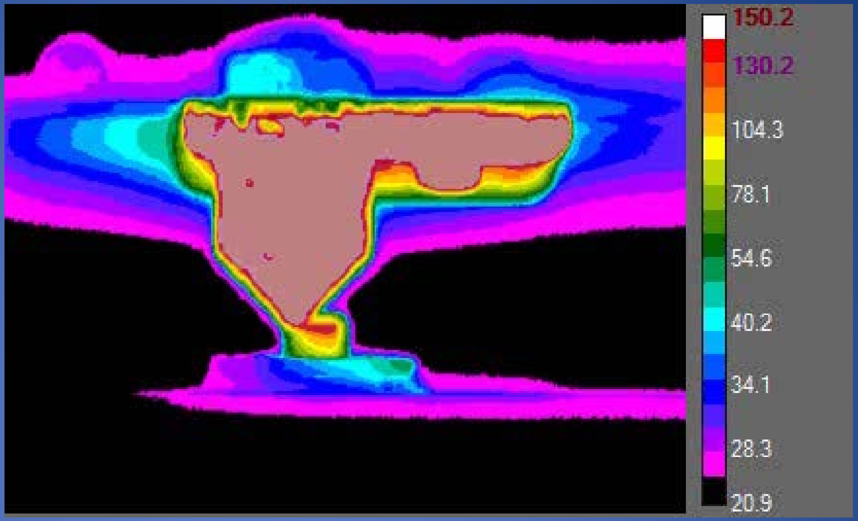
Potential for cell seeding

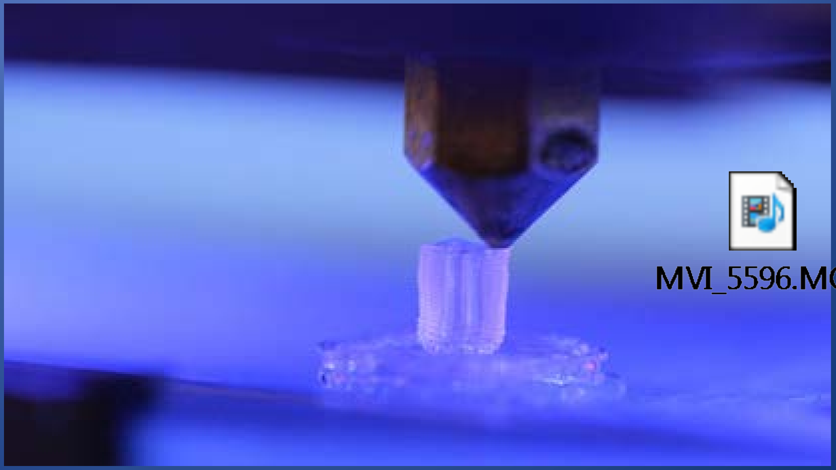
Protein coating (matrix/cytokine)

Images: Courtesy of M Abboud

3D Printing with PLA







Simulating Thermoplastic Flow through a 3D Printer Nozzle

Jake Lindberg, Shibo Chen, Marvin Huang

Chemical Engineering Program, Stony Brook University, Stony Brook, New York, 11794

nozzle

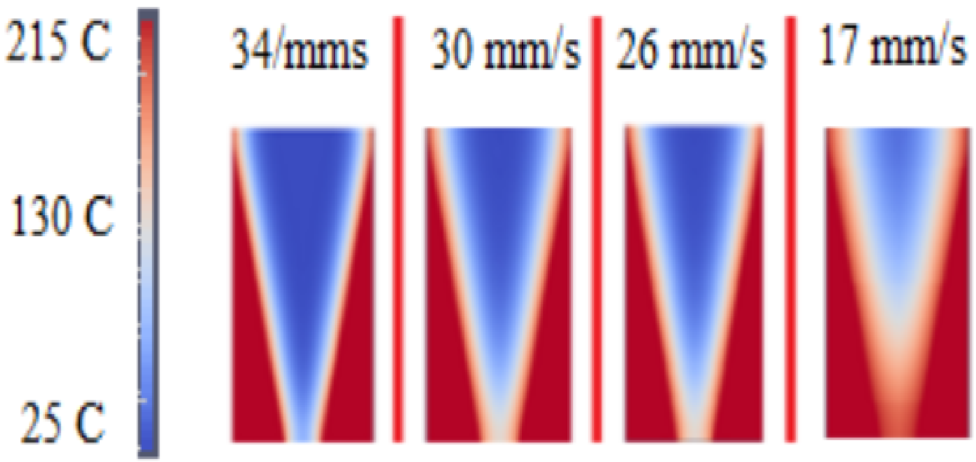


Figure 6. Depiction of temperature distribution from C++ code at tested flow rates. Red indicates a temperature of 215 °C and blue indicates 25 °C.

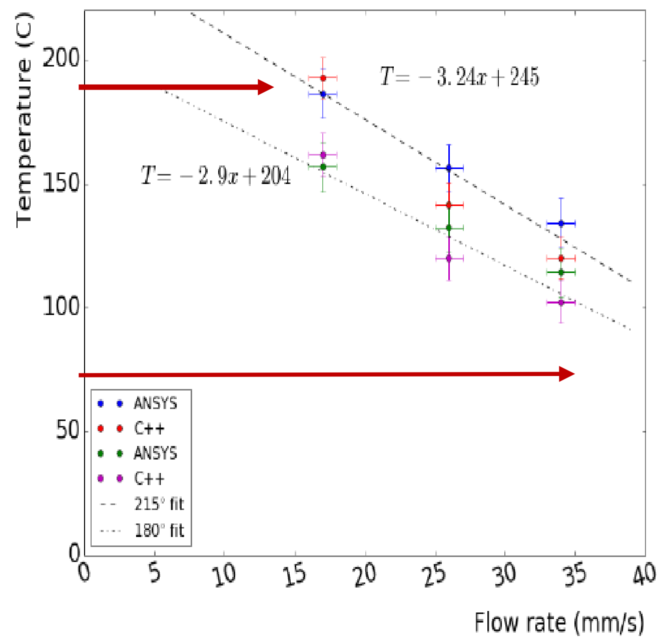


Figure 7. Plot of temperature of extruded polymer along the centerline at the three tested feed rates with extrapolated linear fit.

Figure 1: Extruder geometry.

- Solve Navier-Stokes equation with Advective component.
- Output temperature depends on flow rate.
- Printer runs very close to Tm or Tg.

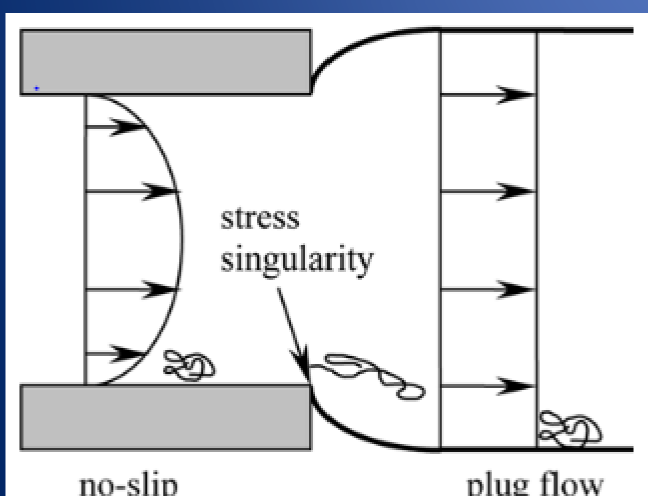
Potential differences between 3D printed and molded surfaces

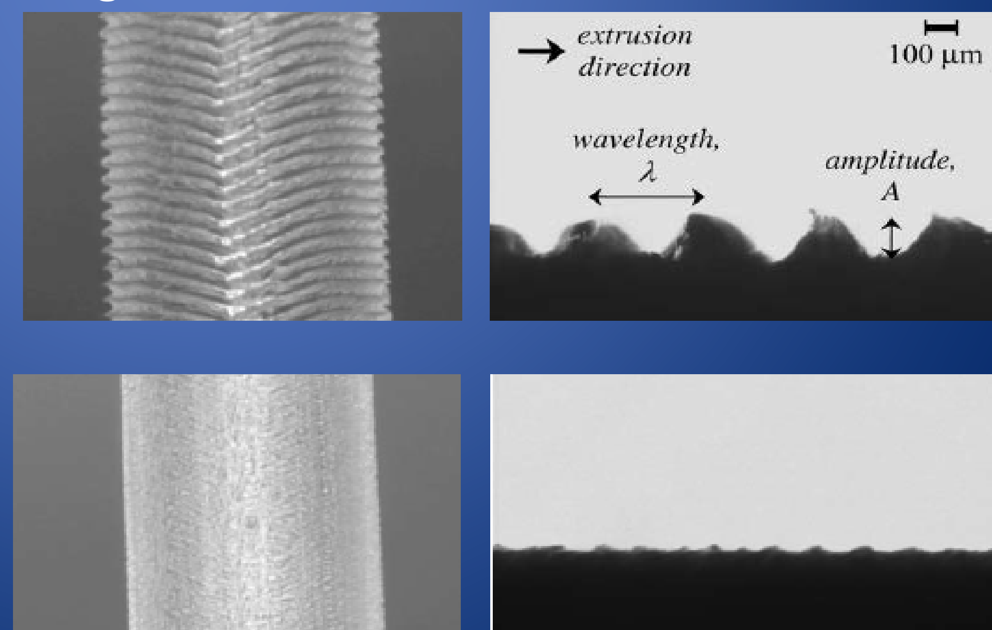
Surface roughness: Sharkskin effect in polymer fibers

E Miller, JP Rothstein, Rheol Acta (2004) 44: 160–173

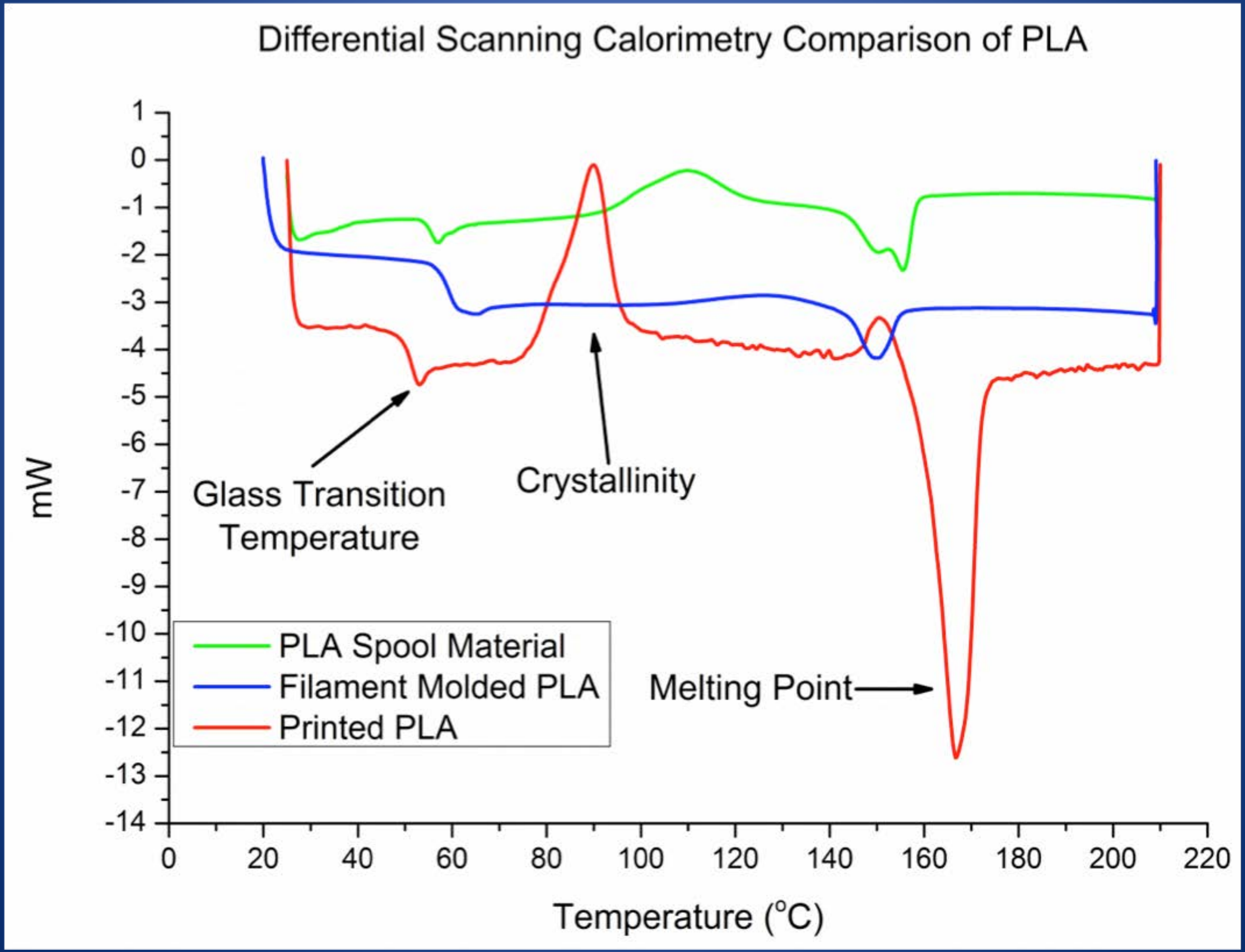
Well known stick/slip instability in flow of polymer filaments as they extrude through narrow nozzles.

- Caused by surface interactions between entangled polymers and the nozzle wall.
- Modulated by adjusting the extrusion rate and the nozzle temperature.

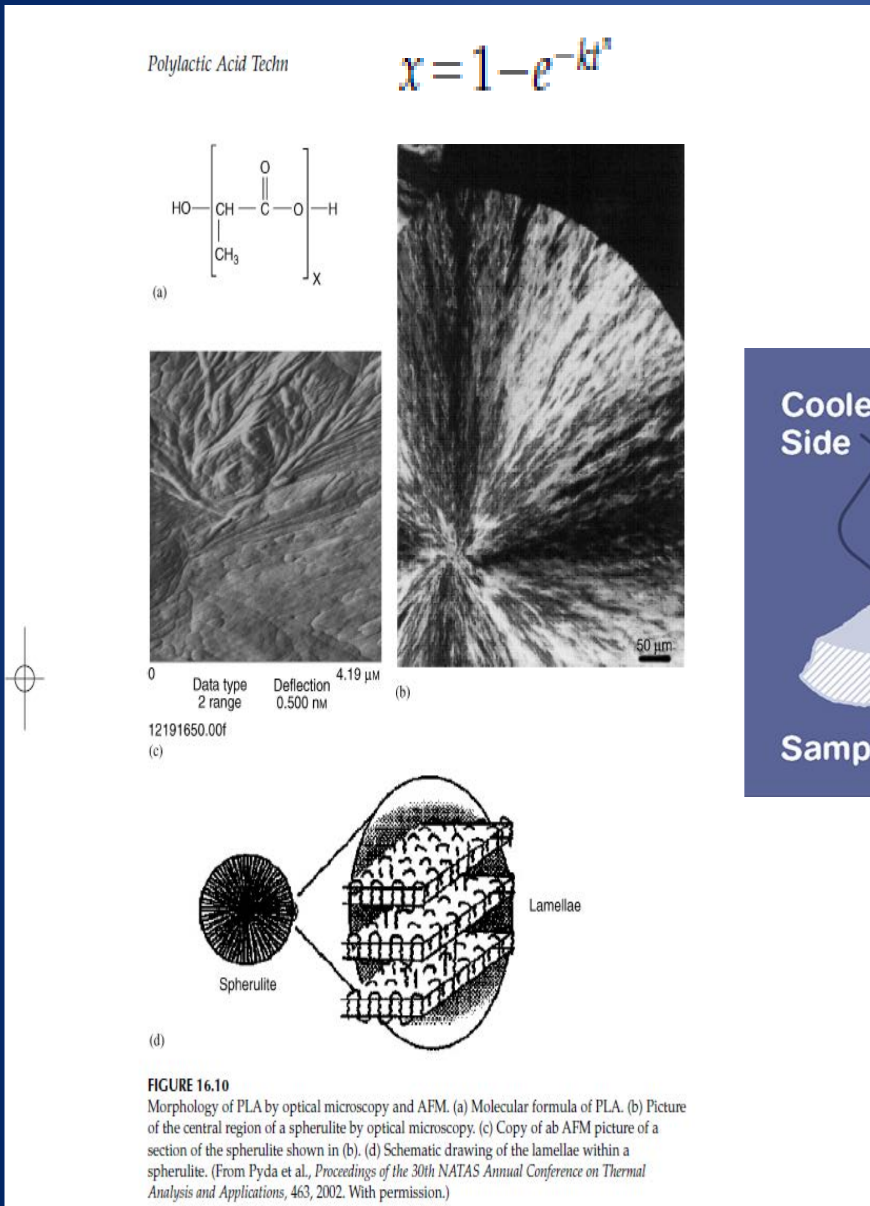




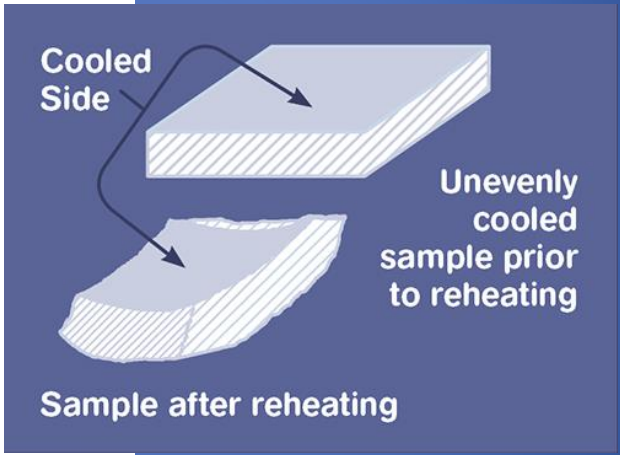
Differential Scanning Calorimetry

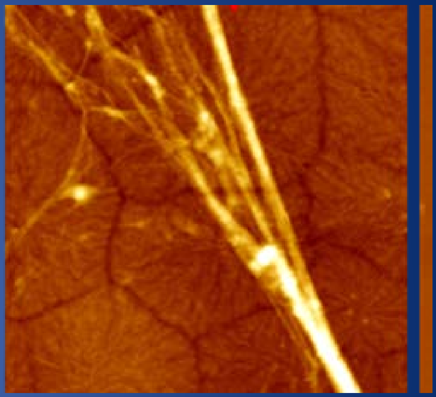


Crystalinity: Kinetics of spherulite formation



- Function of cooling rate
- Nucleation sites
- Time scale similar to thermal dissipation of printer





Provides strength
Defects /faults crack propagation
Uneven cooling warps
Increased surface roughness

A solution spinning

_PBOPPA_solution_spinning

chinaPLA crystalinity filaments

New Window

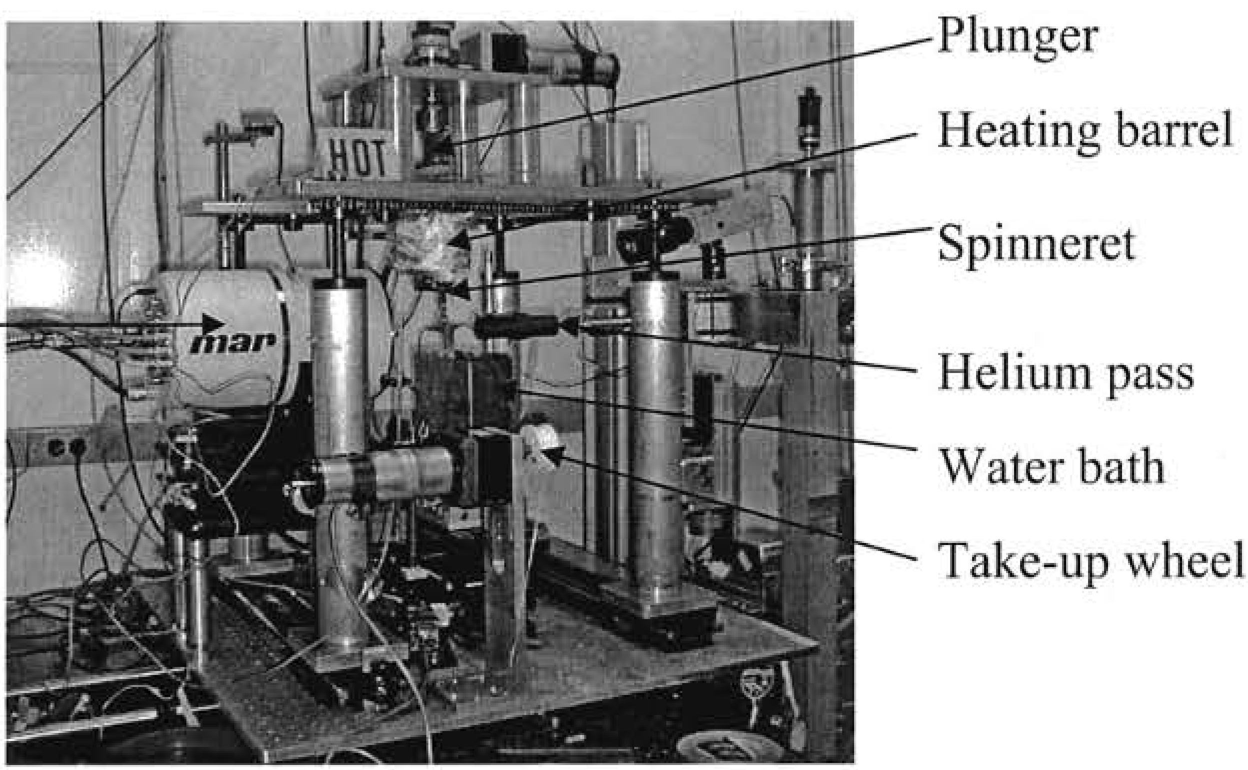
AXD/SAXS studies of structural
3O/PPA solution spinning

9 · January 2002

In-Situ SAXS WAXS

- Map crystallinity
- Map temperature
- Measure crystallization dynamics as a function of temperature

Macromolecules, Vol. 35, No. 2, 2002



f the PBO in-situ spinning apparatus with MAR CCD detector at the beamline X27C in NSLS, BNL.

tal structure[25] It is not clear during the different stages of the process and how

Topics that need further discussion

- Dynamics of crystallization under conditions far from equilibrium
- Effect of surface mechanics and roughness on protein adsorbtion, cell attachment, proliferation, and differentiation.

Front. Mater. Sci. 2012, 6(1): 47–59
DOI 10.1007/s11706-012-0154-8

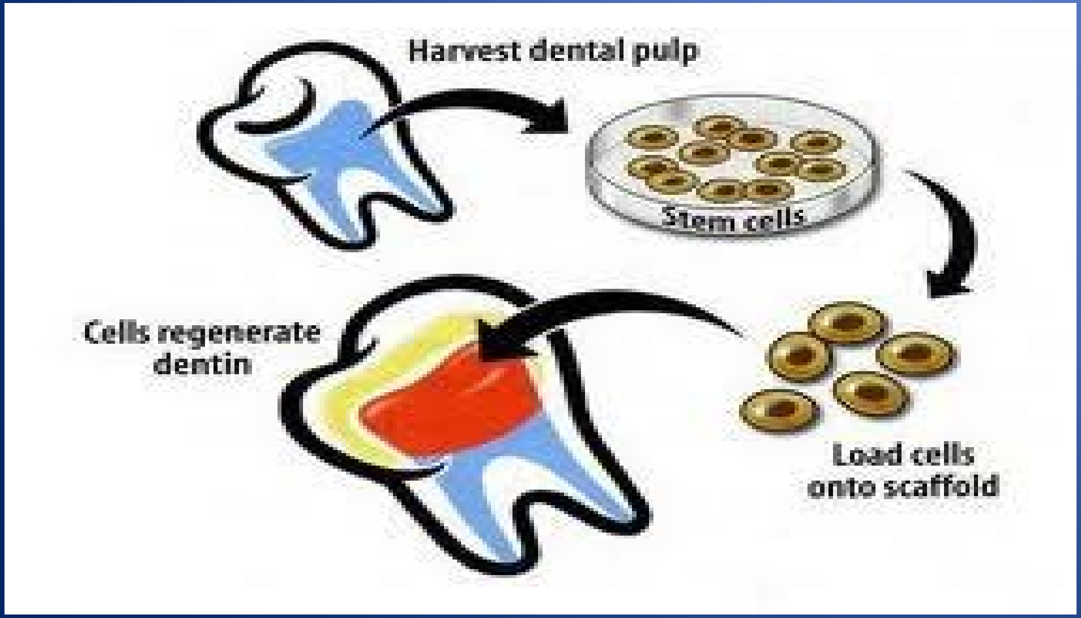
RESEARCH ARTICLE

The role of crystallinity on differential attachment/ proliferation of osteoblasts and fibroblasts on poly (caprolactone-co-glycolide) polymeric surfaces

Helen CUI (✉)[1,2] and Patrick J. SINKO[2]

1 Advanced Technology and Regenerative Medicine (ATRM), LLC, Somerville, NJ 08876, USA
2 Department of Pharmaceutics, Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ 08854, USA

Goal: Regenerate teeth



→ **To develop a biocompatible method for autologous dentin regeneration which combines printed scaffolds with stem cell differentiation.**

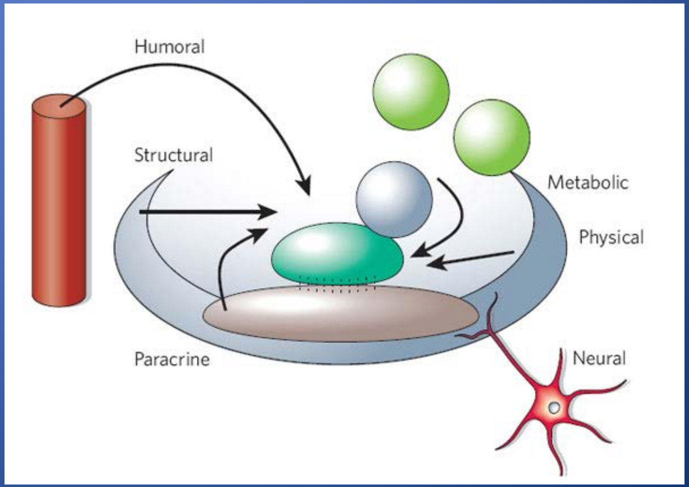
Cells and their niche

Cell Substrates

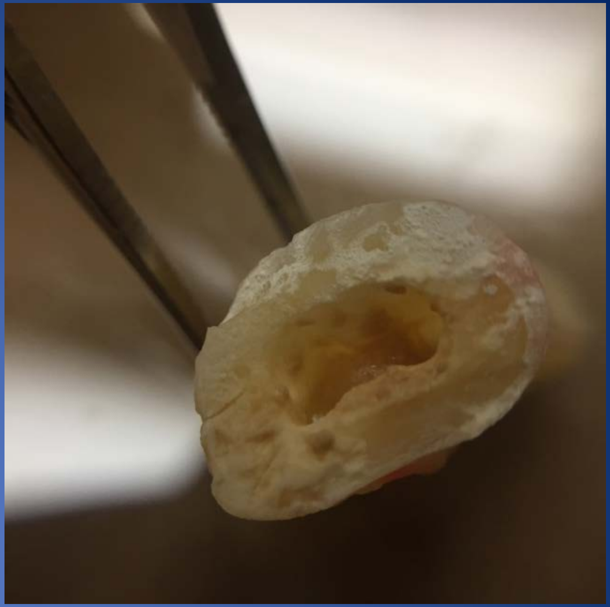
- Mechanics
- Topography
- Chemistry

Soluble and cellular mediators

- Cytokines and growth factors
- Cell associated ligands and receptors
- Tissue fluid (media)



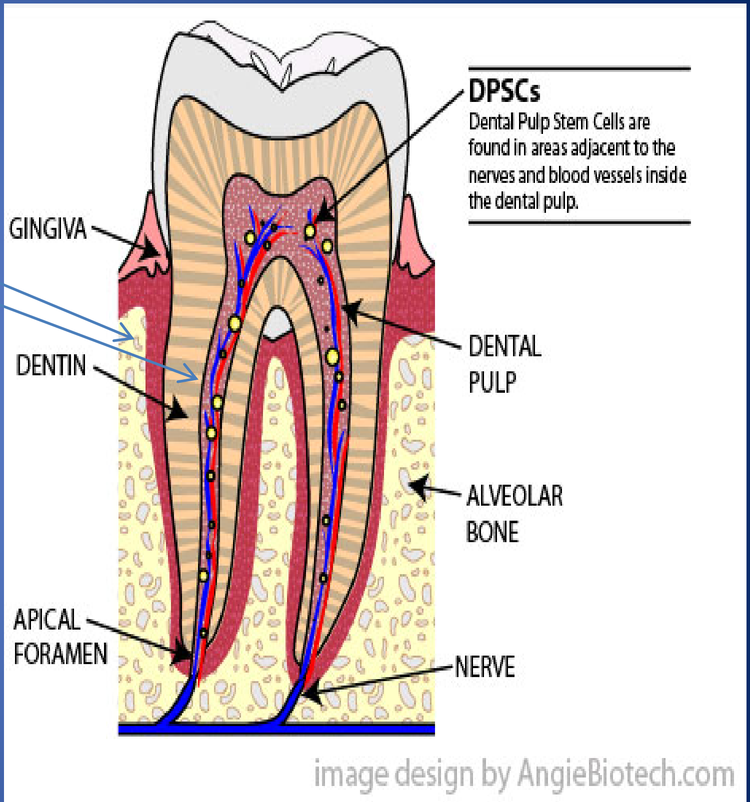
Scadden 2006, Nature 441:1075-79



CELL SYSTEM: DENTAL PULP DERIVED CELLS

Cell Source: Dental Pulp Stem Cells(DPSCs)

Dental Pulp Stem Cells differentiate → Osteoblasts
Odontoblasts
Adipocytes
Neuronal Cells
Muscle Cells
Cartilage (chondrocytes)

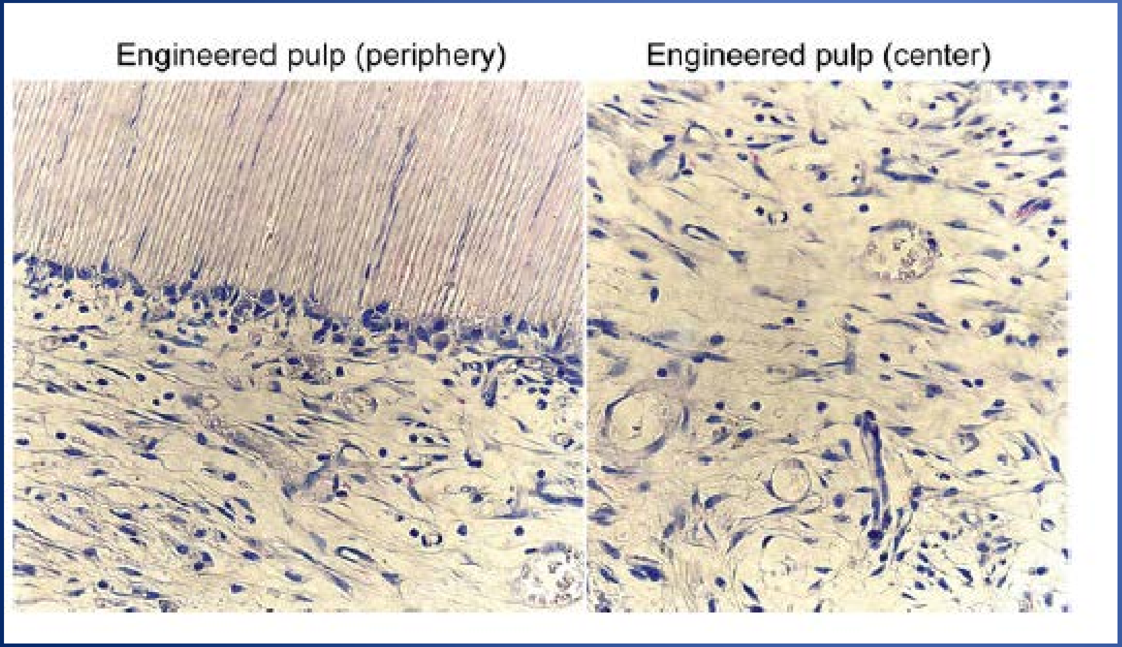


DPSCs were chosen for the study because of
- Their easy accessibility
- high efficiency of extraction procedure
- faster multiplication rate
- their ability to self-renew *in vivo*

For this study, DPSCs were isolated under IRB approval # 20076778.

Induction: Dexamethasone(Dex /DXM)

- DPSC can be chemically induced with high doses of dexamethasone (glucocorticoid steroid) to differentiate into osteoblasts (in vitro) [1]
- Steroids (unnatural) have adverse side effects i.e. weakened immune system and hyperglycemia [2]



Special challenge in the tooth :

- Confined space in the canal
- Difficult to localize soluble factors
- High degree of order
- Cells must sense very small changes in substrate

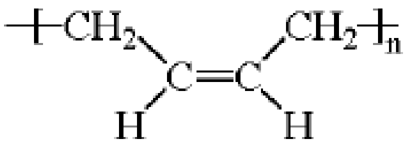
[1] "Dexamethasone stimulates differentiation of odontoblasts like cells in human pulp cultures", Alliot-Licht et al., Cell Tissue Res (2005) 321.

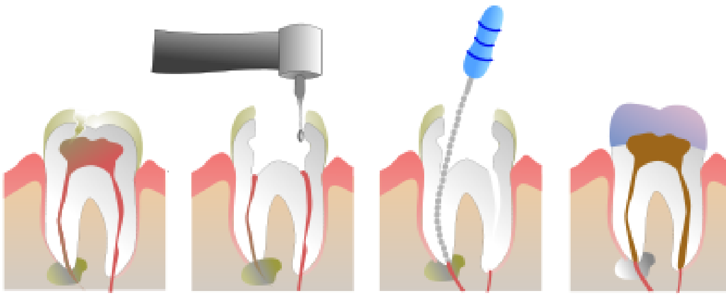
[2] " Differential Effect of Glucocorticoids on Calcium Absorption and Bone Mass", Gennari C. et al., Rheumatology 32.2(1993):11-14, Oxford Jornals.

Polymeric substrate:

Polybutadiene (PB)

- Physical properties
  - Mw = 205,800
  - Mw/Mn = 1.49
  - Tg = -95℃
- It is rubber-like at room temperature.





- Biocompatible
- Similar to Polyisoprene
- Used to obdurate root canal (same as tires).
- **Re-engineer for pulp regeneration rather than obduration.**

Malcolm Steinberg (1930-2012)

R.A. Foty, M.S. Steinberg / Developmental Biology 278 (2005) 255–263

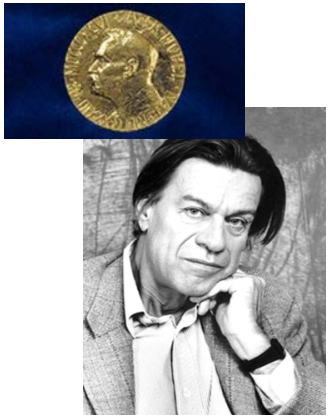
Abstract: The differential adhesion hypothesis (DAH), advanced in the 1960s, proposed that the liquid-like tissue-spreading and cell segregation phenomena of development arise from tissue surface tensions *that in turn arise from differences in intercellular adhesiveness*. ……**without exception, a cell aggregate of lower surface tension tends to envelop one of higher surface tension to which it adheres**

" Malcolm was My Biologist" Lecture at NYU Poly --2006

Pierre-Gilles de Gennes (1932-2007)

The Nobel Prize in Physics 1991

Nobel Lecture, December 9, 1991: "SOFT MATTER"
A related (although more complex) system of this type is a red blood cell. For many years it had been known that, when observed under phase contrast, these cells flicker. - …. The essential property of insoluble bilayers is that they optimise their area at fixed surfactant number. **Thus, the energy is stationary with respect to area: the surface tension vanishes**.



Embryonic Stem Cells Sense Mechanics of their Environment:

- Labeled outside shell and core cells of embryo
- Dissociated cells and allowed them to re-assemble
- Cells self assembled correctly into core-shell
- Shell cells had lower surface tension or number of cadherins

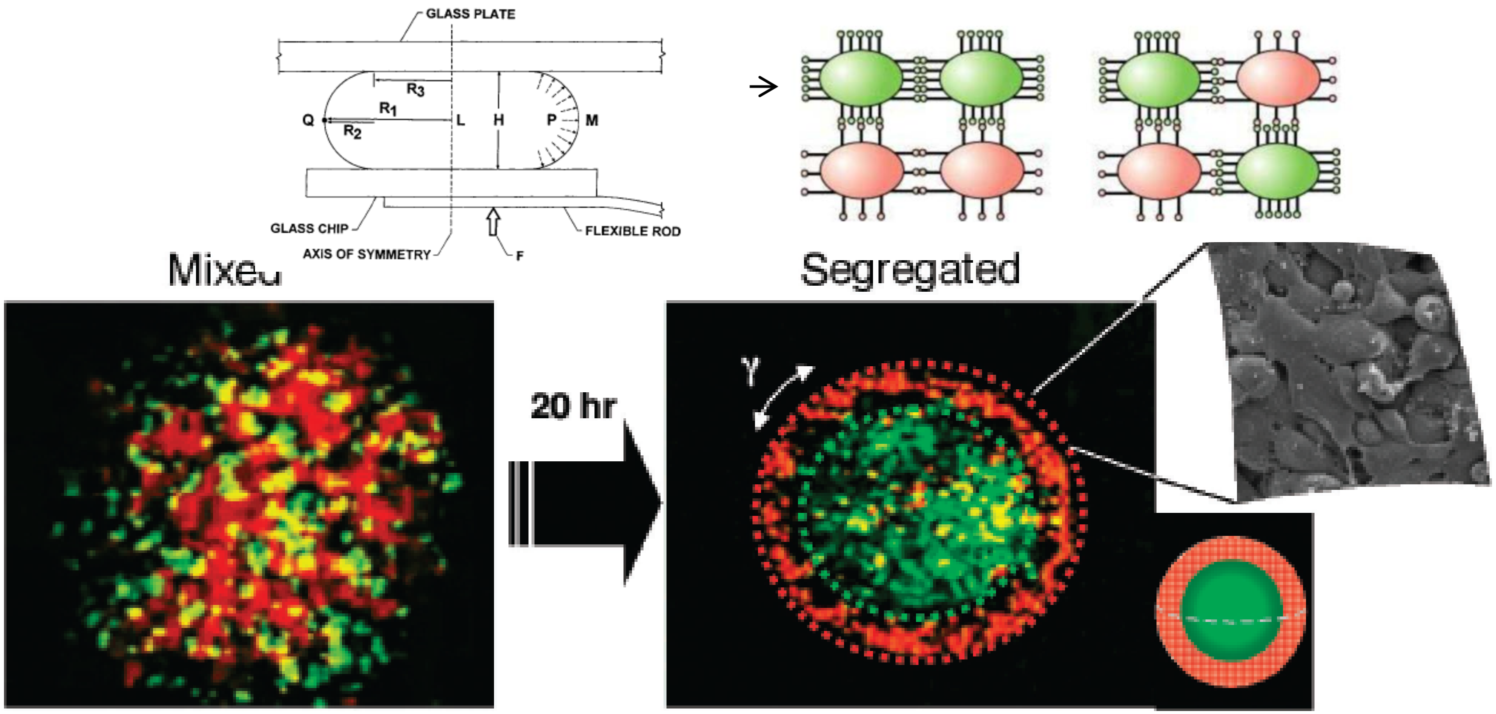


Fig. 4. Sorting of two cell types into a 3D shell-core aggregate (~300 μm in diameter) in which low expressers of N-cadherin (labeled in red) surround high expressers of N-cadherin (labeled in green) (73). Scanning electron micrograph of a typical spheroid's surface shows well-spread cells. [Adapted from (73) with permission from Elsevier. Image courtesy of G. Forgacs, University of Missouri]

R. A. Foty, M. S. Steinberg, *Dev. Biol.* 278, 255 (2005).

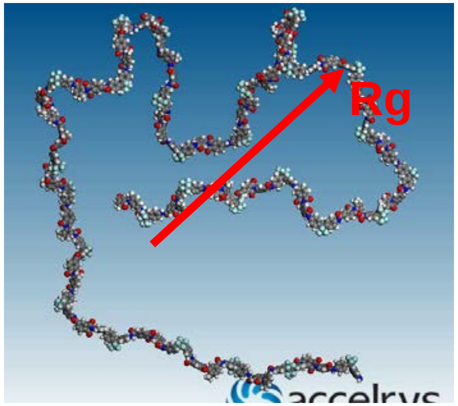
Davis, Phillips, and Steinberg

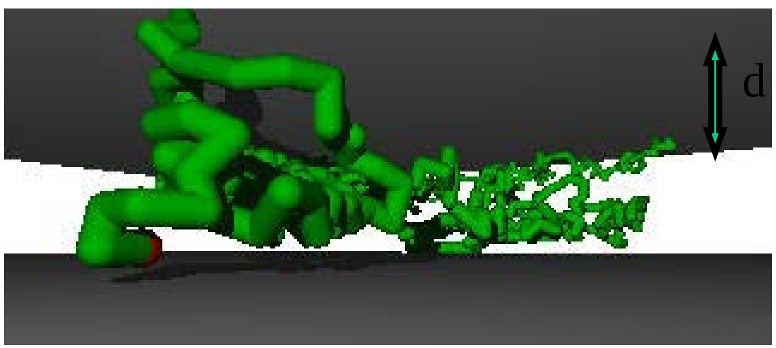
DEVELOPMENTAL BIOLOGY **192**, 630–644 (1997)
ARTICLE NO. DB978741

$$R_g = \frac{1}{\sqrt{6}} \sqrt{N}\, a$$

Elastomer: Why are they special?

Kurt Binder website





- **We can control chemistry and mechanics separately.**

•S=kT (d/R^2) -> Loss due to confinement or cross linking.

- Confinement and surface interactions determine visco-elastic properties.
- Radius of Gyration:

$$R_g = \frac{1}{\sqrt{6}} \sqrt{N}\, a$$

P.G. DeGennes Scaling concepts in polymer physics, Ithaca, N.Y, Cornell University Press (réimpr. 1985),

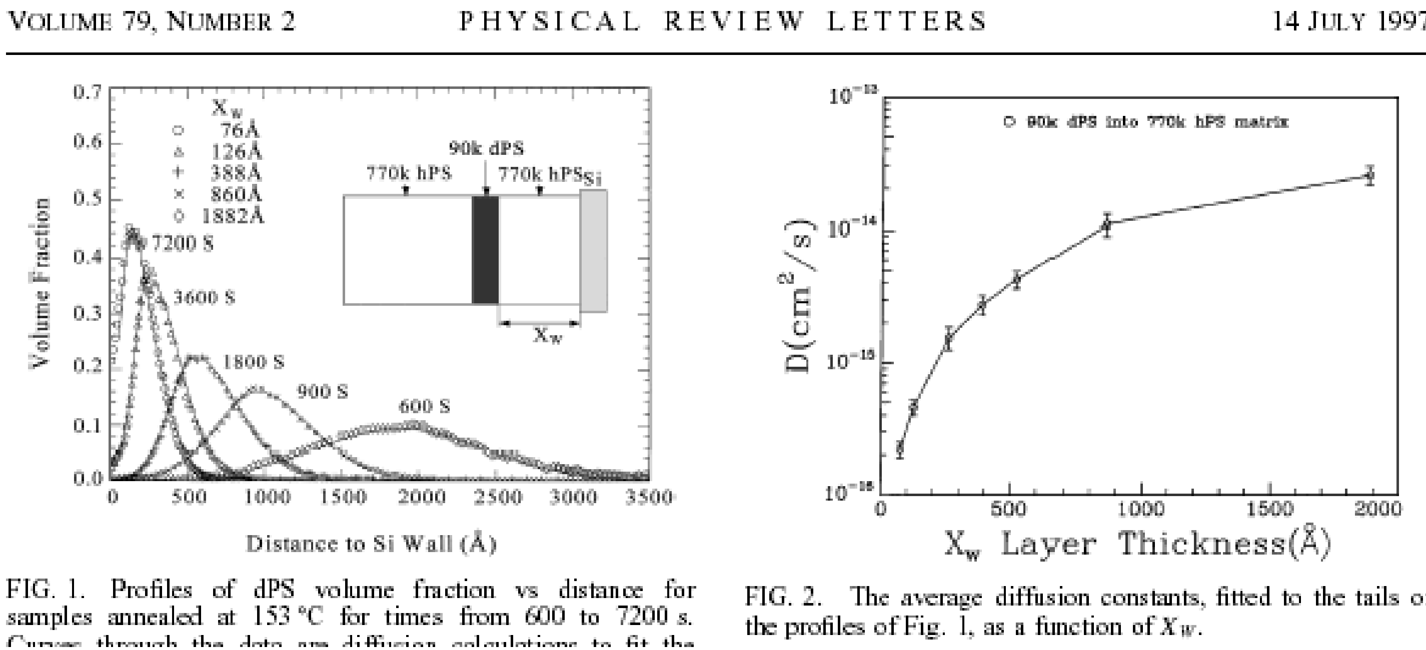
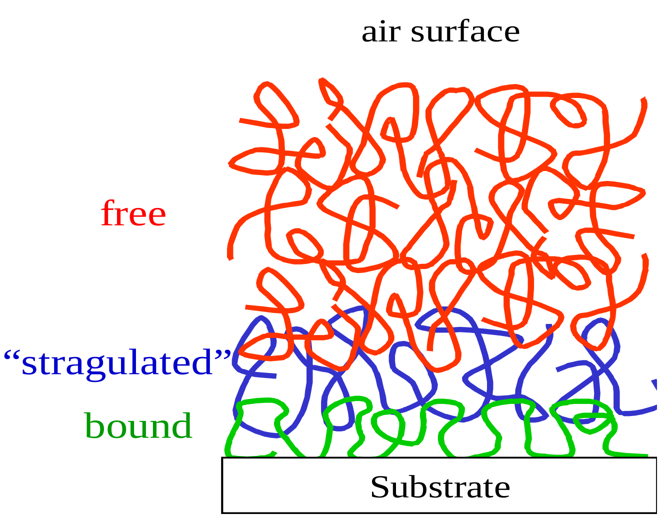

VOLUME 79, NUMBER 2 PHYSICAL REVIEW LETTERS 14 JULY 1997

FIG. 1. Profiles of dPS volume fraction vs distance for samples annealed at 153 °C for times from 600 to 7200 s. Curves through the data are diffusion calculations to fit the

FIG. 2. The average diffusion constants, fitted to the tails of the profiles of Fig. 1, as a function of X_W.

D~kT/η

Einstein relation



Two Fluid Model:

D=Do Nc/Ne in a X-linked matrix.

N $^{1/2}$ surface contacts~ Nc for surface

Predictions: (1) D~N $^{3/2}$ (2) N $^{1/2}$ ~Nc for Mw~4M (3) Surface effect propagated by entanglements in range; Ne<N<4x10 ^{4}

Predicts Scaling for Modulus: Resistance to Deformation and Viscous Flow

Influence of Radius of Gyration: Rg~sqrt (Mw)

- Gaussian Chains form N1/2 contact with surface
- If attached then they act as cross-linkers,

D=Do (Nc/Ne)

- Ne=sqrt (N) for Mw~10 6 for PS
- ONLY when Ne=Nc surface effect is removed.

interface. The reptation model expression [22] is $D = (k_B T N_e / 3N^2 f_0)$, where k_B is Boltzmann's constant, T = temperature, N_e = number of monomers between entanglements, N = number of monomers per chain, and f_0 is a monomeric friction coefficient. Polymer conformations enter through N_e and certainly might be different close to the wall. Bruinsma [23] has considered

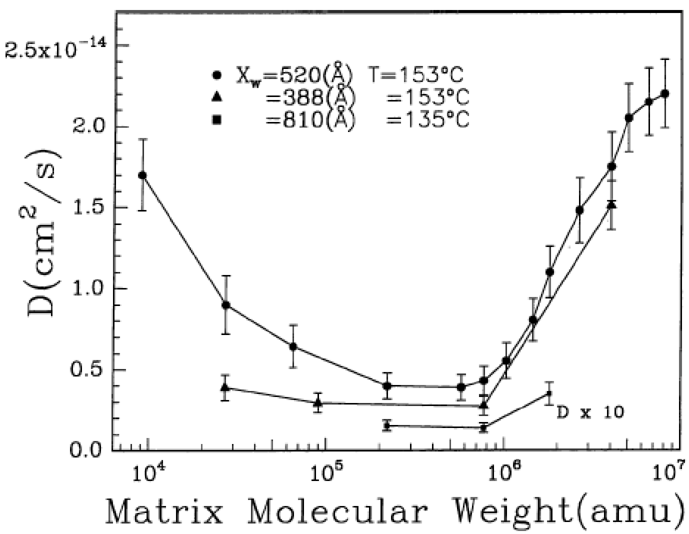


FIG. 3. The average diffusion constants of 90 × 10^3 dPS at 153 °C as a function of hPS matrix molecular weight for various X_W thicknesses. Sample geometry as in Fig. 1.

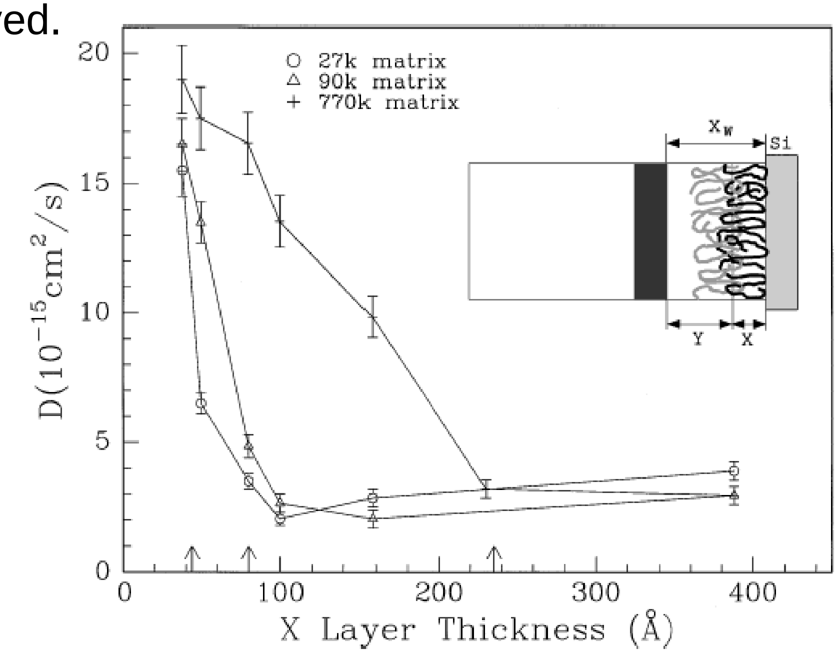
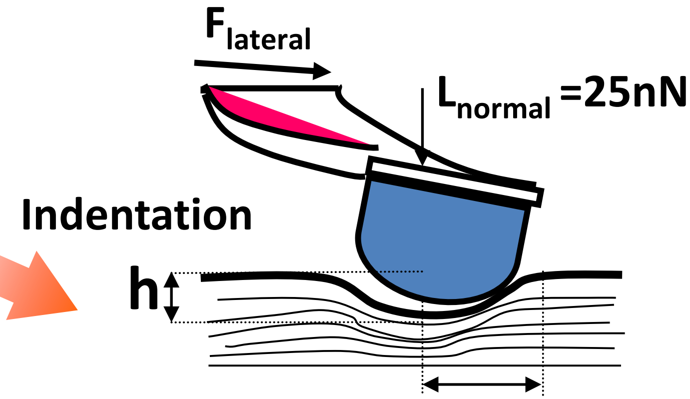
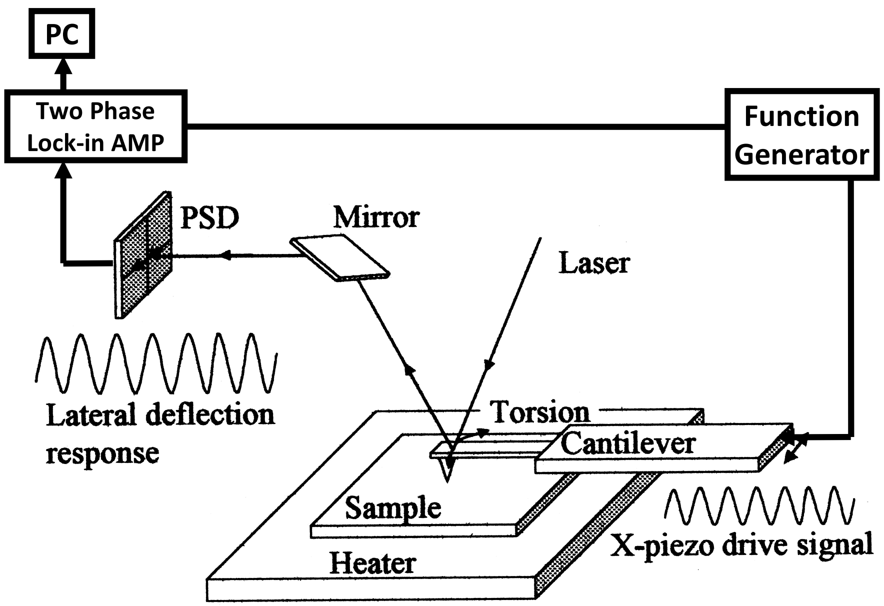


FIG. 4. Results of split layer experiments for X_W = 388 Å showing the diffusion coefficient of 90 × 10^3 dPS at 153° for various X layer thicknesses. Inset shows sample geometry. Arrows indicate R_g values for the 27 × 10^3, 90 × 10^3, and 770 × 10^3 hPS matrix polymers.

Atomic Force Microscope

$$D = \frac{3}{4}\frac{1-\upsilon^2}{E}, \Delta x \sim h = \left[D \frac{L}{R^{1/2}} \right]^{\frac{2}{3}}$$





Displacement $\Delta x \sim h$

h: Tip indentation

E: Modulus of material

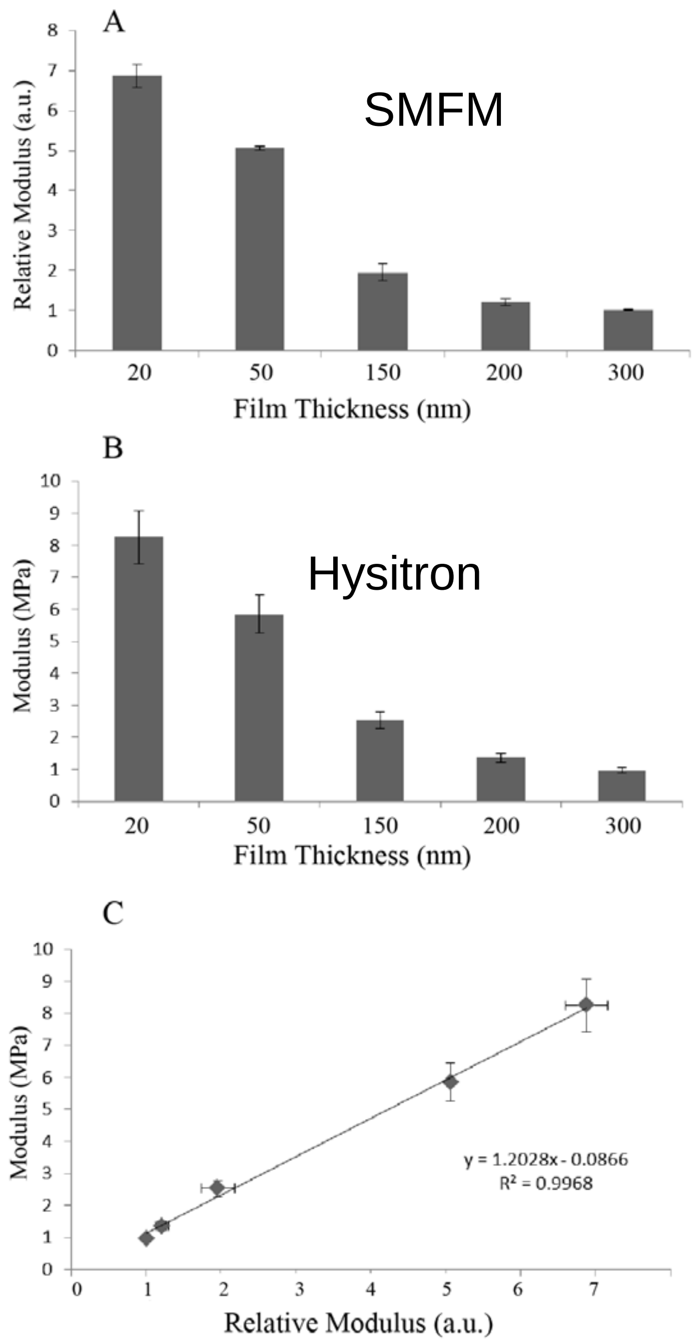
ν: Poisson ratio

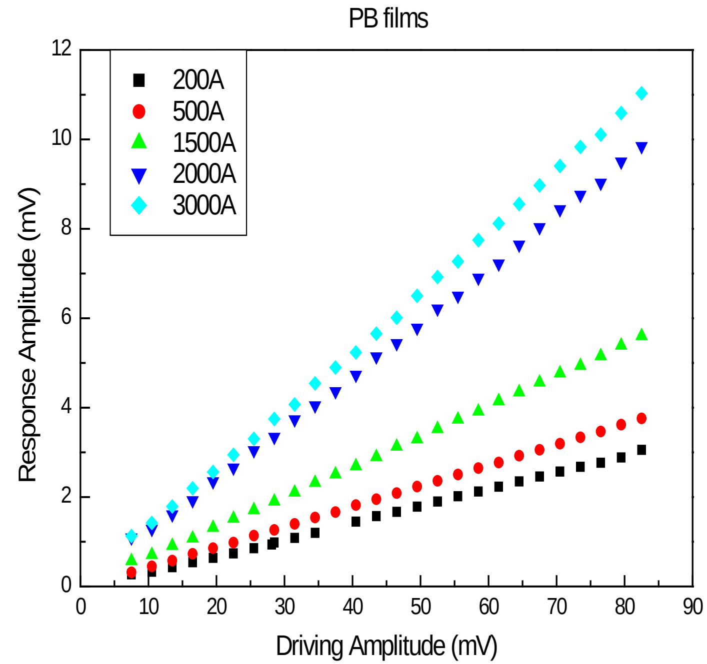
R: Tip radius

L: Cantilever length

- At T=Tm sample melts and becomes soft.
- Tip contact area increases.
- Indentation increases (h).

- Δx increases sharply
- Friction increases
- Measure Tm





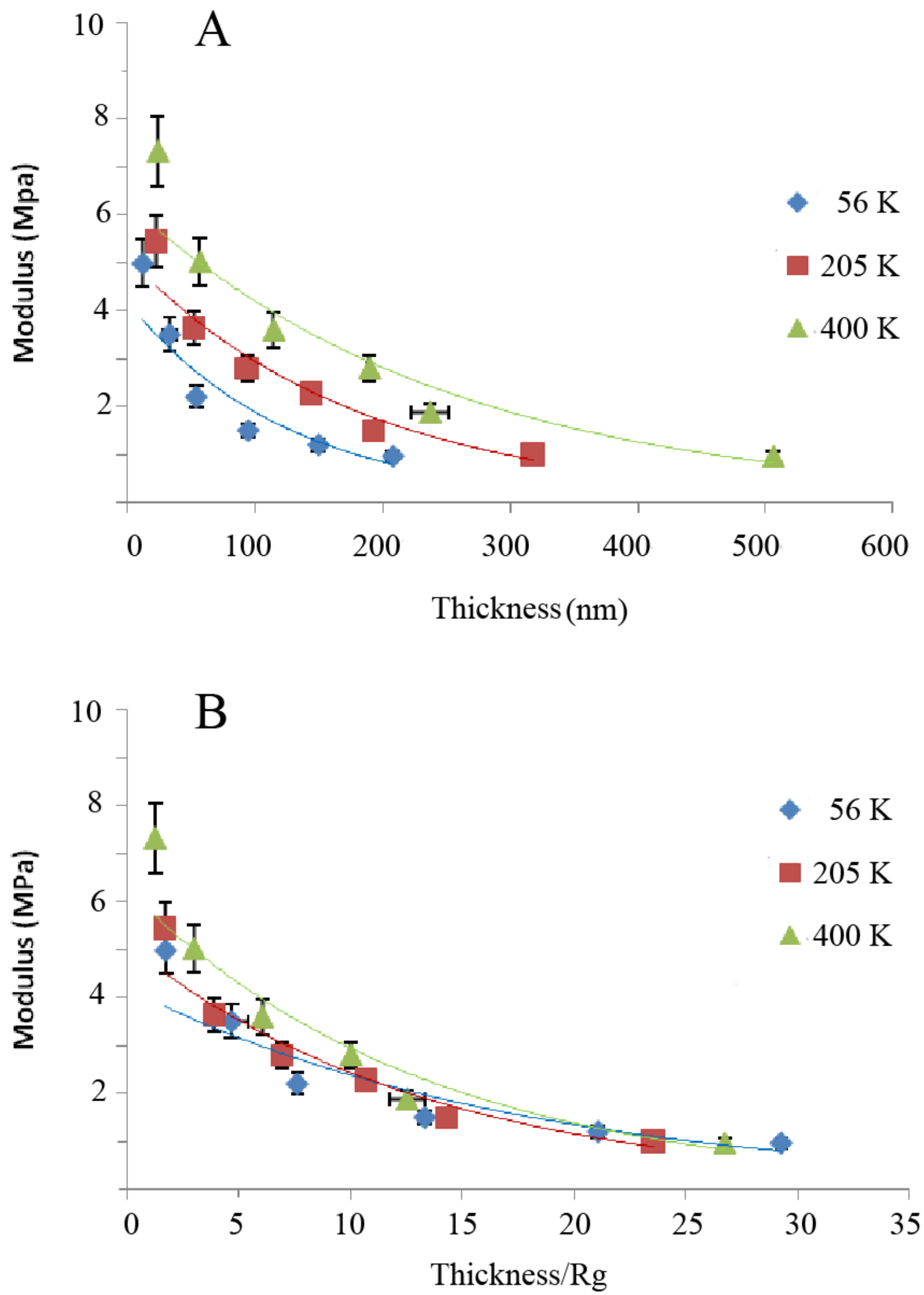
$$\frac{G_t}{G_0} \sim \left(\frac{\Delta X_0}{\Delta X_t}\right)^{1.51}$$

G : shear modulus

ΔX: lateral deflection

- Modulus decreases with increasing film thickness.
- Allows for variation of one order of magnitude.

Y. Ji, B. Li, S.Ge, J.C. Sokolov, M. Rafailovich, *Langmuir* 2005, 22, 1321-1328

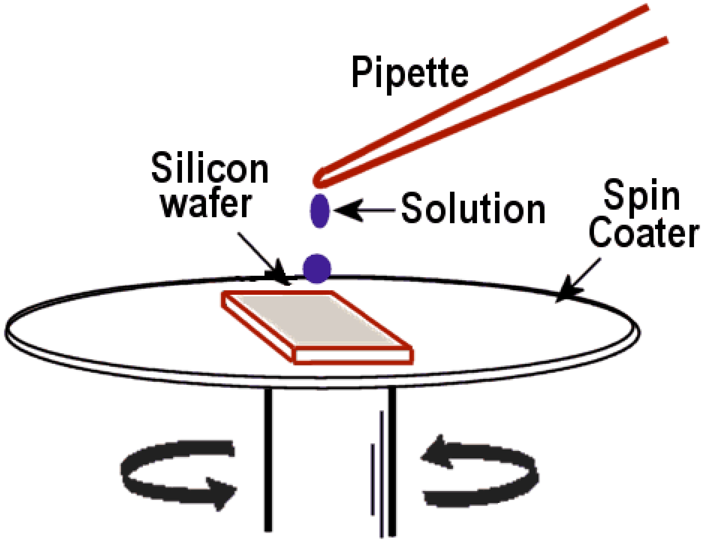


Molecular Weight Effect on Modulus:

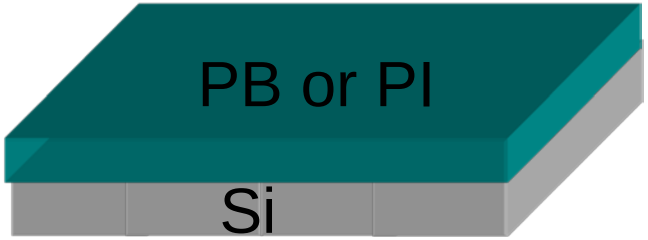
Is the modulus effect a function of Rg?

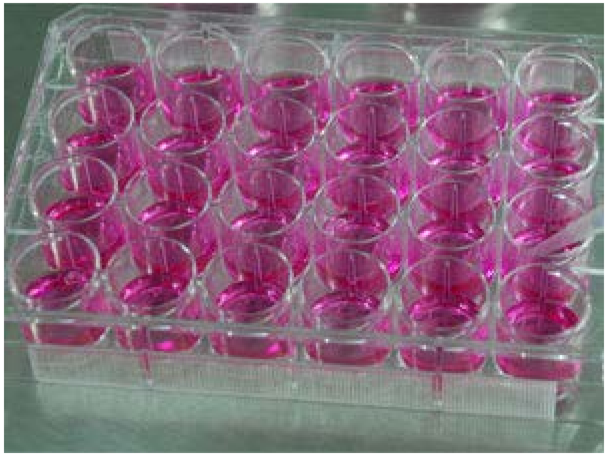
- Modulus decreases exponentially with increasing film thickness.
- Same functional form for all Mw-> Scales with Rg.
- Confinement effect: Surface interaction influence on modulus for ~20 Rg's
- Molecular weight: Another variable to increase flexibility of design.

Polymer Film Processing



- Wafers were cut into $1cm^2$ squares
- HF etched Si wafers
- PB spun cast from toluene
- Thickness of 200 to 3000 A were measured by ellipsometry
- annealed in Ultra High Vaccuum (UHV) for 24 hours which prevents dewetting, removes toxic solvent, sterilizes substrates.







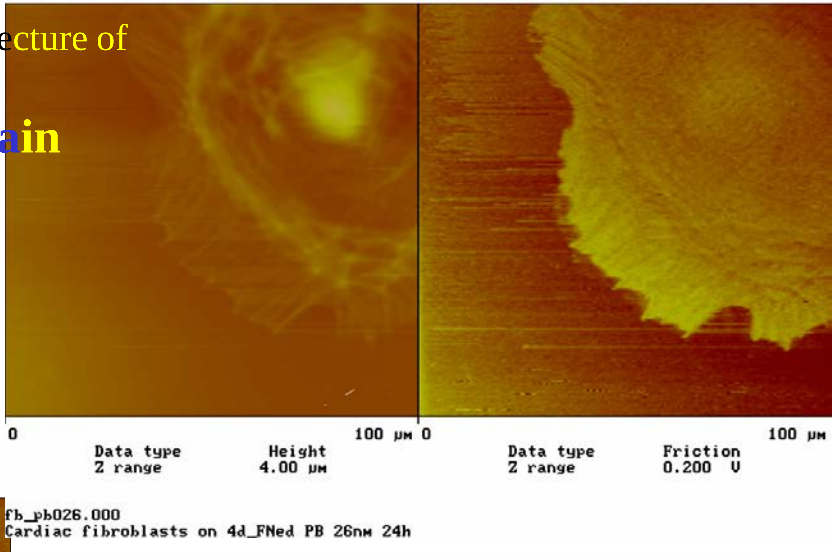
Bio-Tensegrity

840A

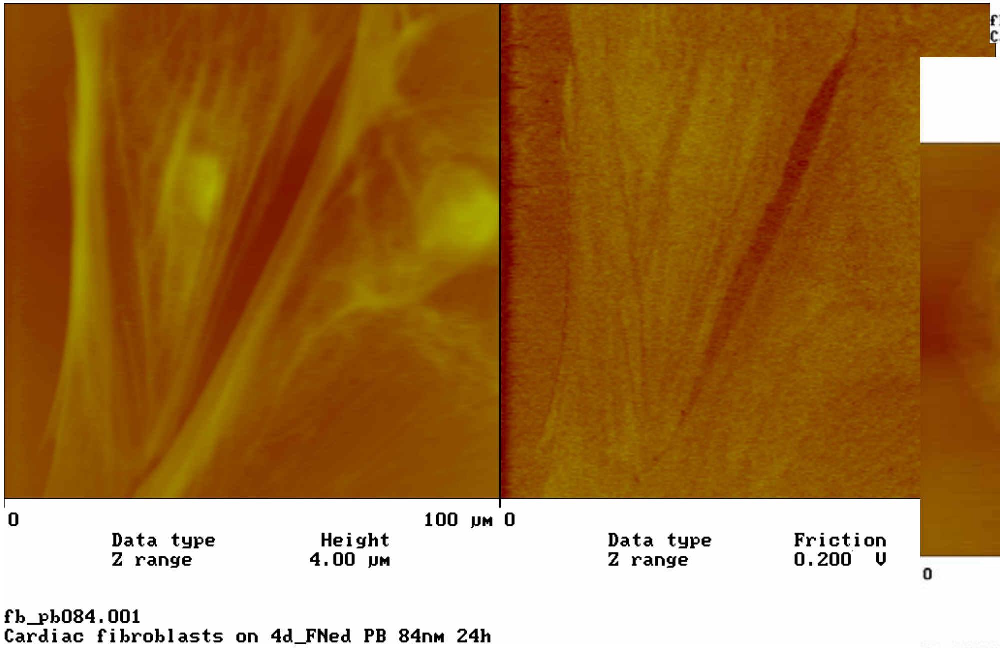
Do cells sense matrix modulus? Ingber, D.E., The Architecture of Life. Scientific American Jan 1998; 278:48-57

Donald Ingber : Cells redistribute stress to maintain tensile integrity.

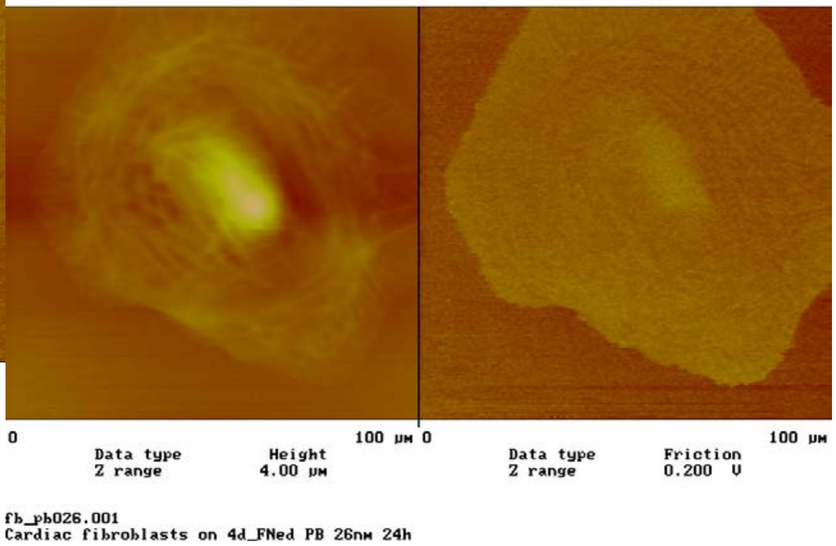
- **No tensile stress across cells surface.**
- **No contrast with substrate**

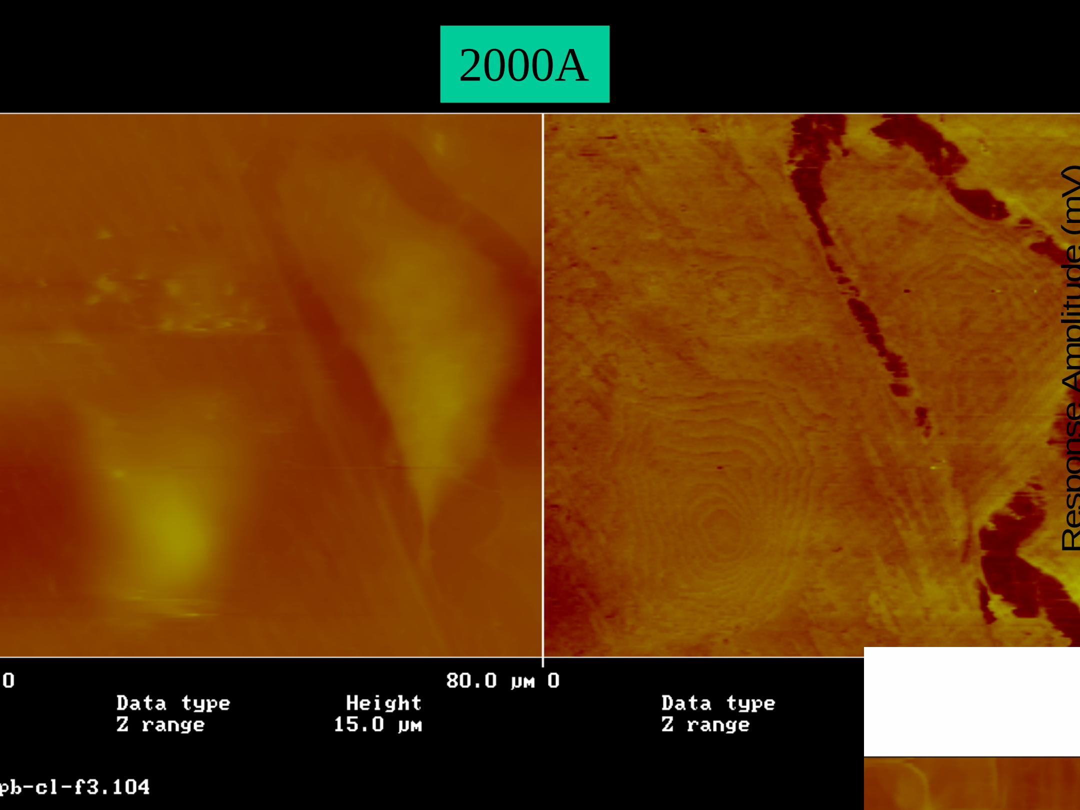


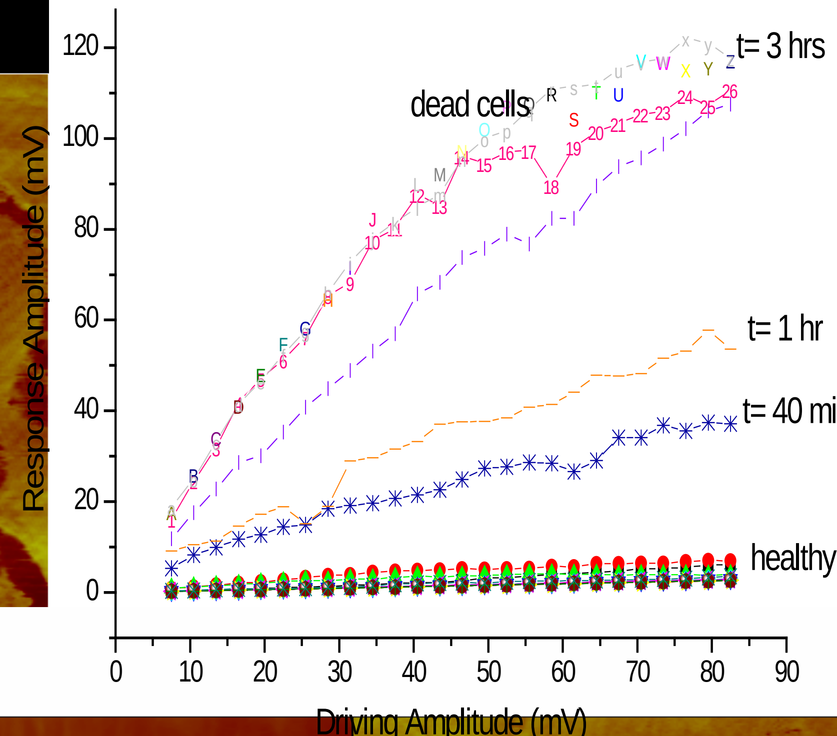
Topography 260A Lateral Modulation



840A

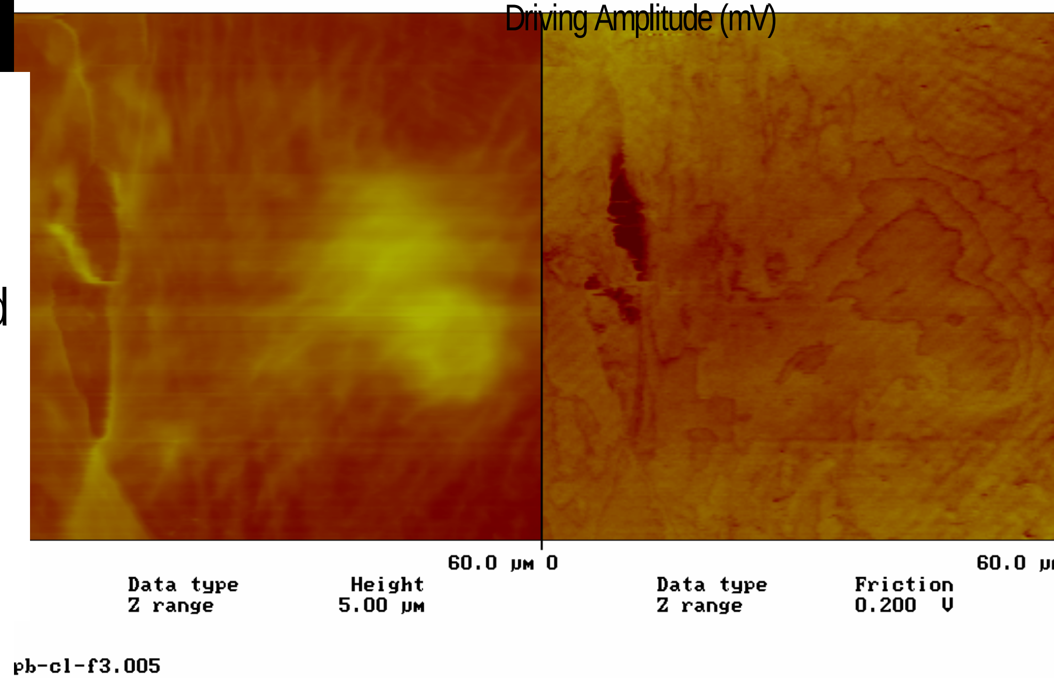




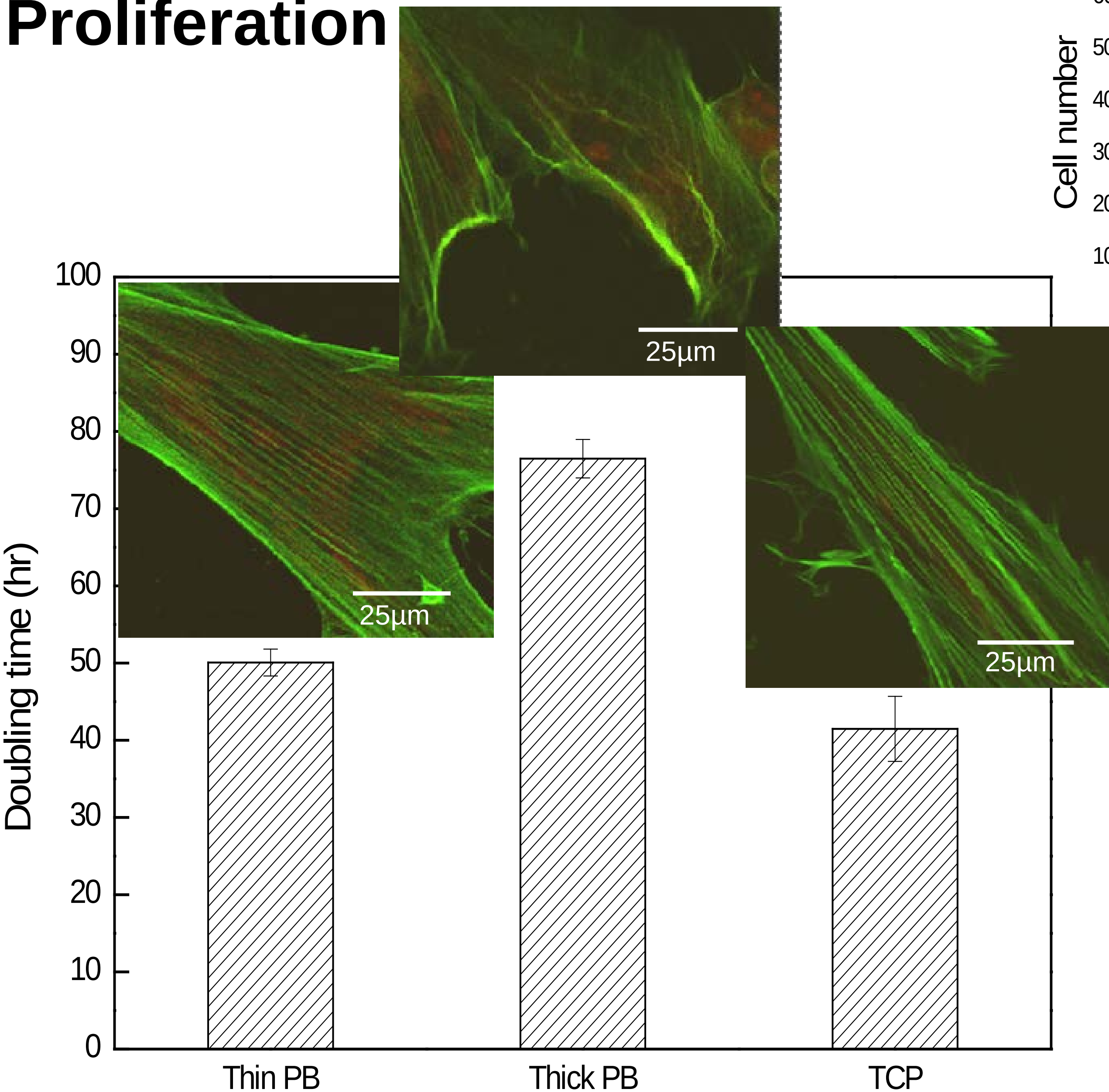


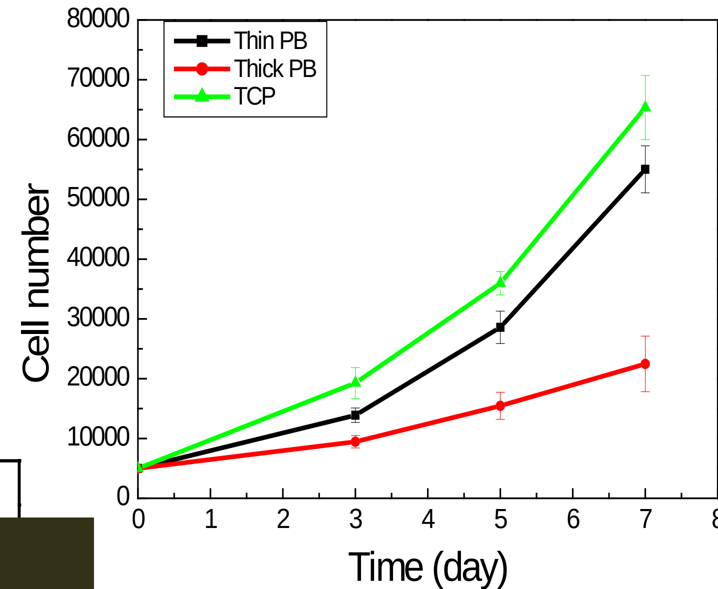
➢Dying Cells

- Effects are observed after 40min in ambient T=23C
- Concentric rings are becoming disordered as cell loses its adhesion to the surface.
- Modulus decreases (cells get softer).
- Contrast with Pb/Si substrate increases.



DPSC on PB: Influence on Proliferation



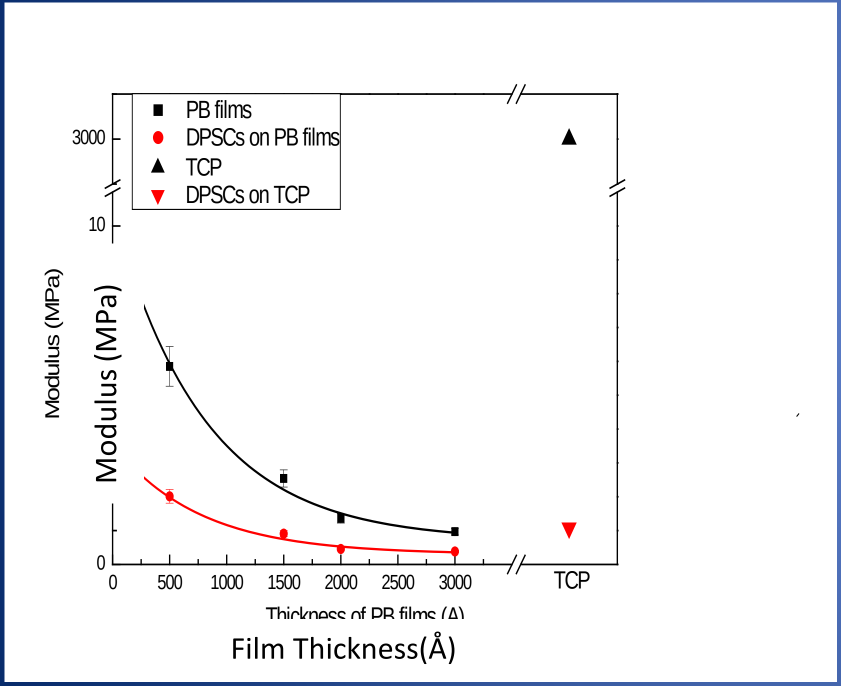


- **Cells like PB.** Proliferation without additional protein i.e. Fn) coating.
- Doubling time is the same on thin PB as TCP.
- **Cells adhere**: Actin is well extended on TCP and thin PB
- PB similar to membrane?

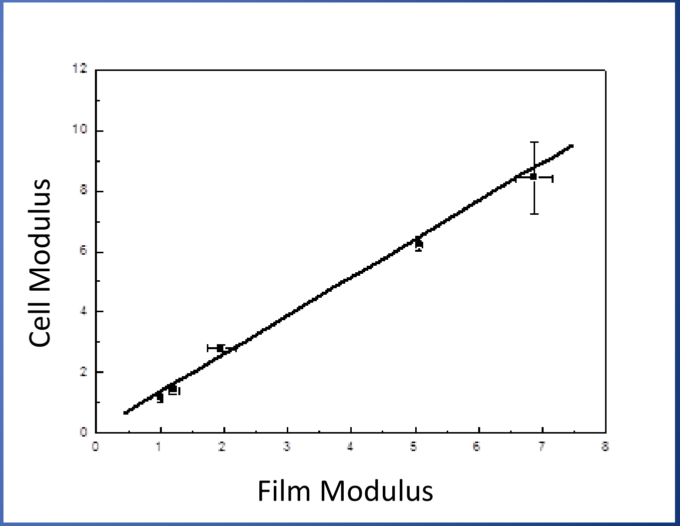
Dental pulp cells respond to surface mechanics:

Cell modulus follows surface modulus

Moduli decrease with film thickness



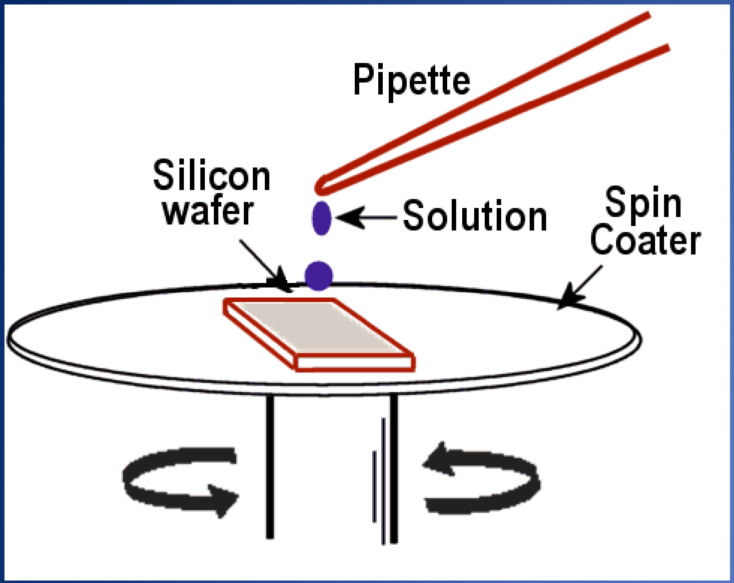
Cell and surface moduli show the same functional form



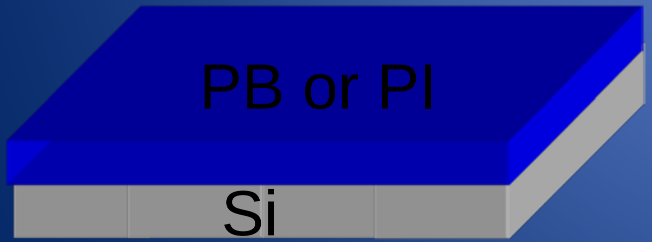
Cells respond to differentially small changes in surface modulus

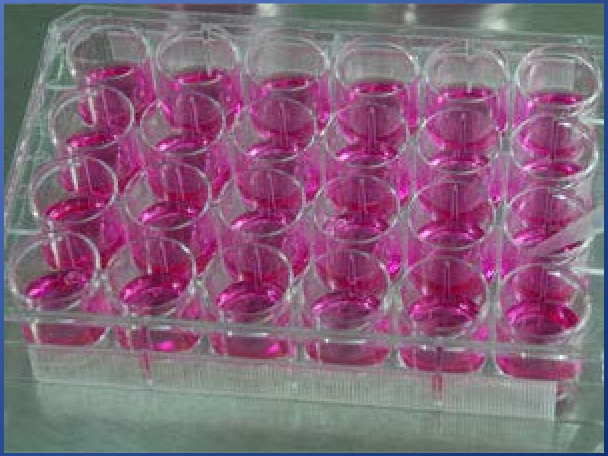
Evaluations using polybutadiene (PB) surfaces:
PB (250K) spun cast out of toluene onto HF treated silicon

Polymer Film Processing



- Wafers were cut into 1cm^2 squares
- HF etched Si wafers
- PB spun cast from toluene
- Thickness of 200 to 3000 A were measured by ellipsometry
- annealed in Ultra High Vaccuum (UHV) for 24 hours which prevents dewetting, removes toxic solvent, sterilizes substrates.

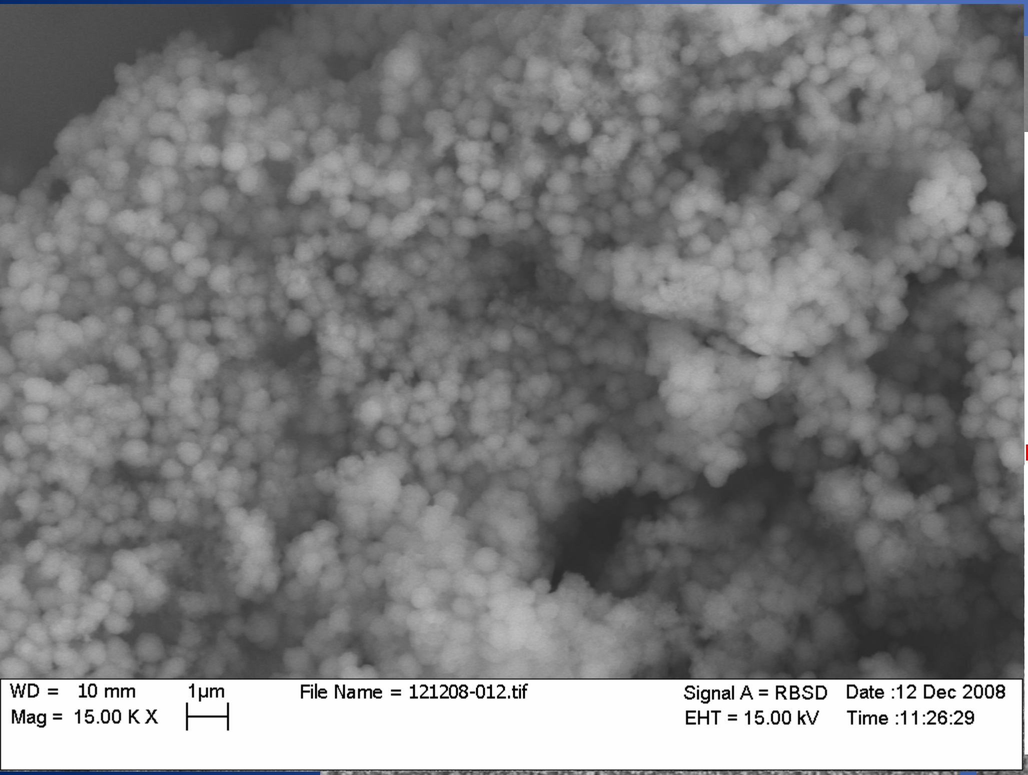


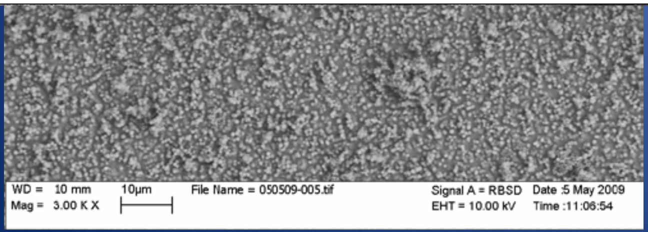


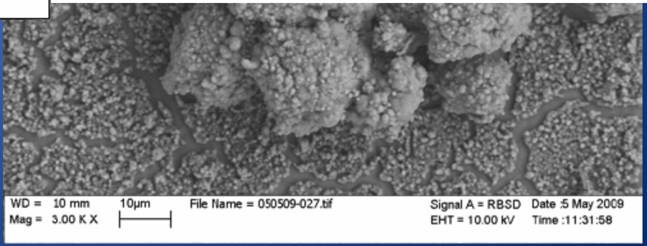
SEM–EDAX of DPSCs on PB films after 21 day incubation

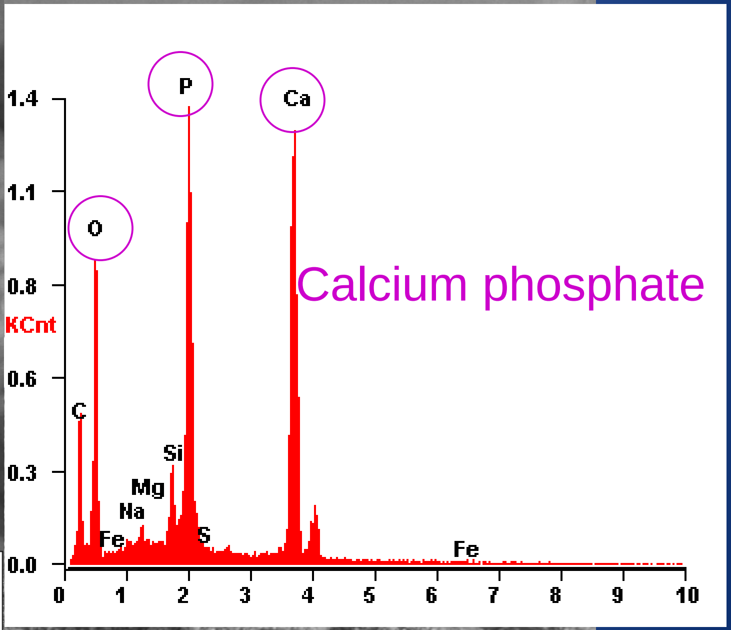
200A

2000A

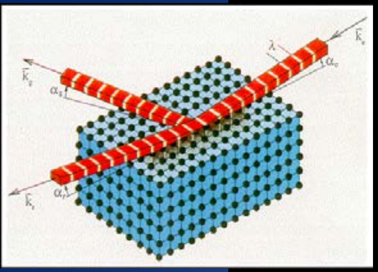


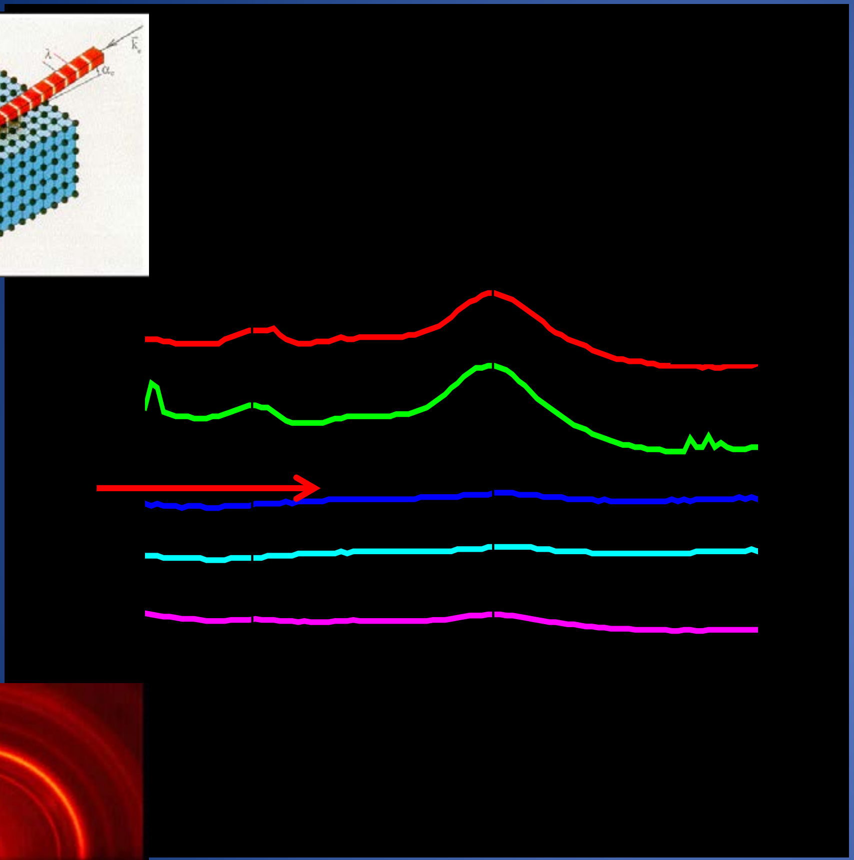


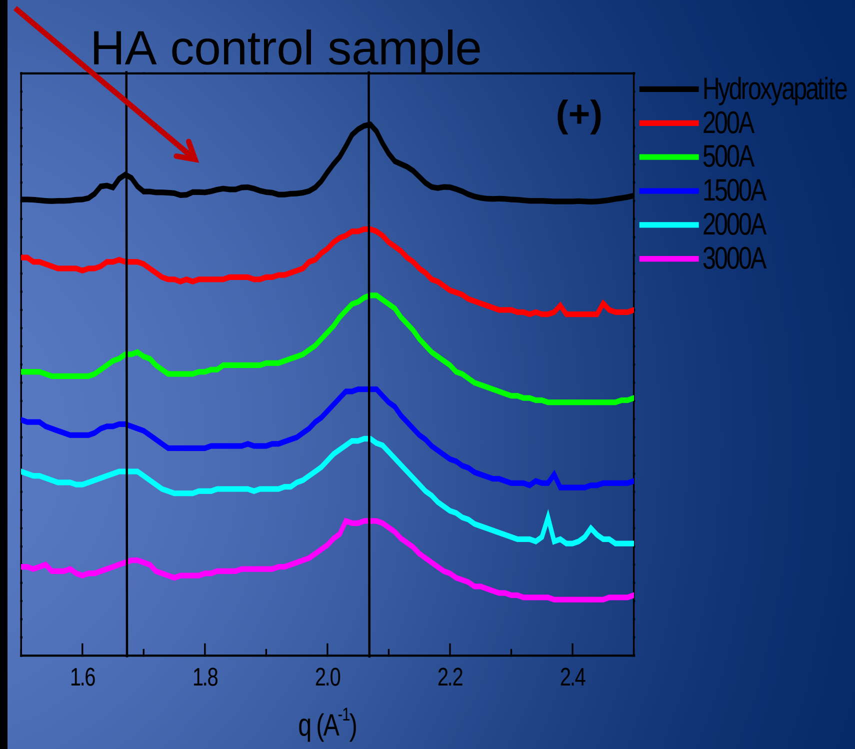




Grazing Incidence X-ray Diffraction (GIXD) of DPSCs on PB films after 21 day incubation







GIXD confirms SEM results;

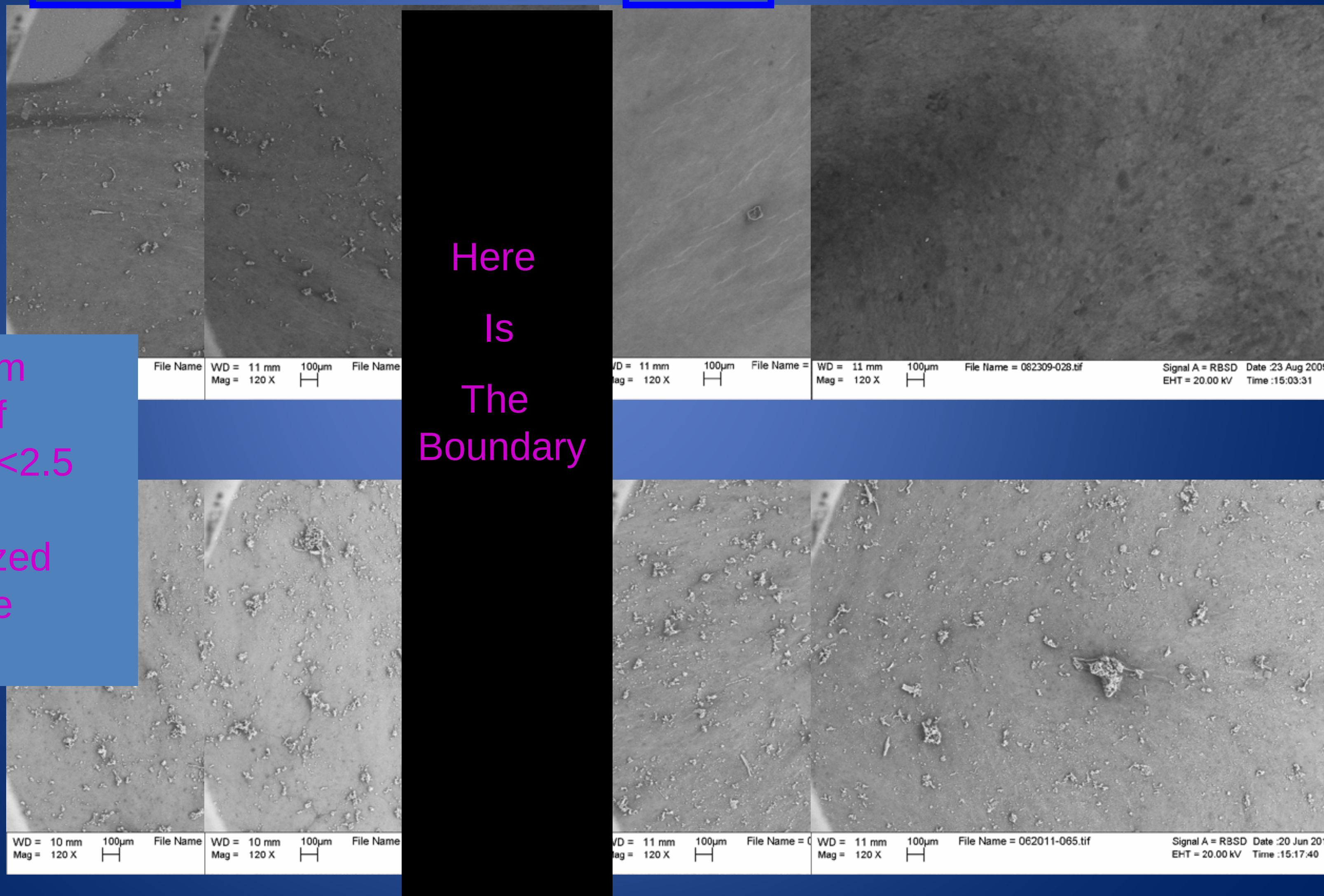
- Diffraction peak positions correspond to crystalline HA
- No crystalline deposits are formed on films 150nm or thicker.

SEM of DPSCs on PB films after 21 days of incubation

200A | 500A | 1500A | 2000A | 3000A

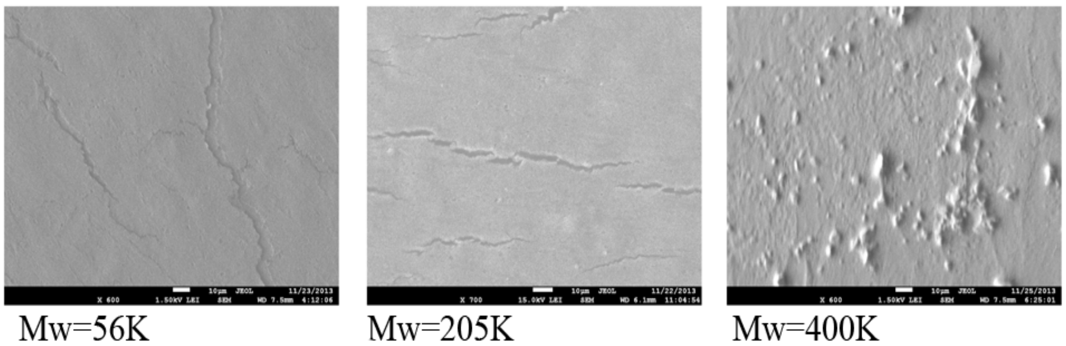
Non-Induced

Induced

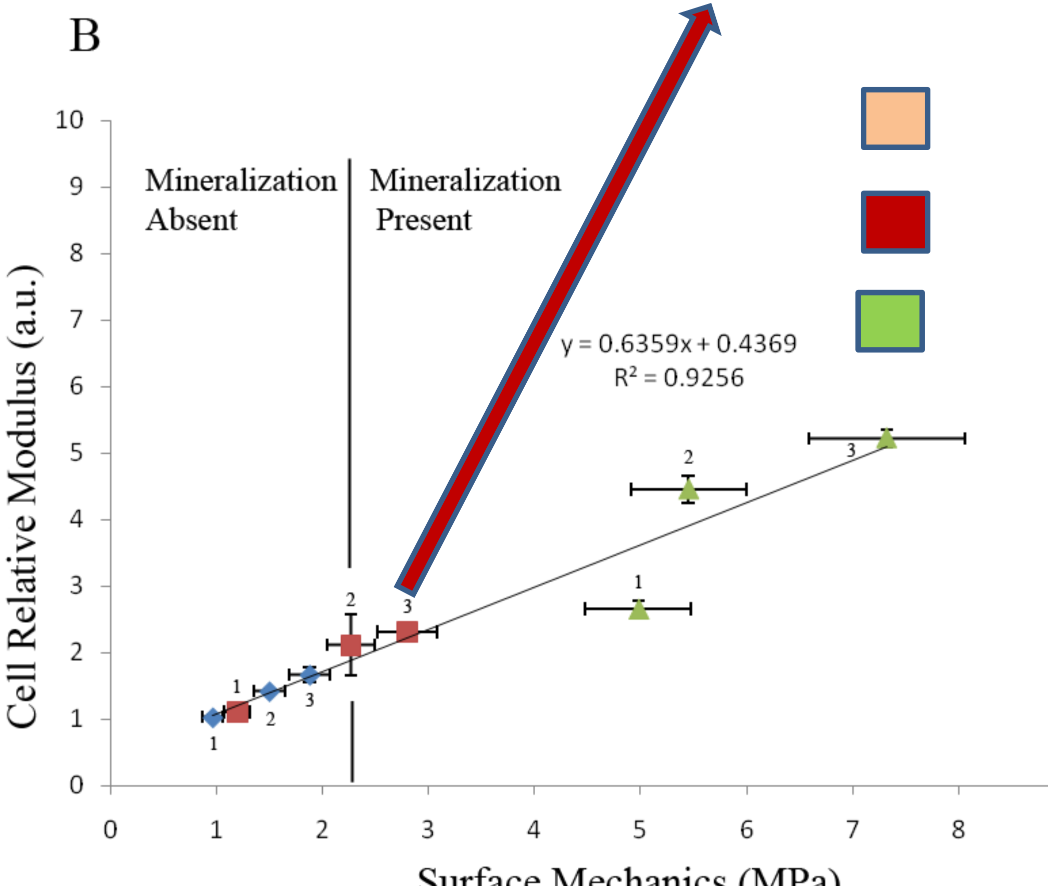


Above a film thickness of 150nm (G <2.5 MPa), no biomineralized deposits are observed.

150 nm thick film:



Do cells sense Rg?



- Cells moduli scale linearly with film moduli; not thickness.
- Cells sense film mechanics, not substrate.
- **Confirm Rg scaling of modulus**

Mineralization Markers involved in DPSCs differentiation

- Osteocalcin (OCN) – marker for bone formation, produced solely by mature osteoblasts [1]

- Bone Sialoprotein (BSP) – specific maker for bone formation, is expressed in very lower amounts (~1%) in dentin and large amounts (~8-12%) in bone [5]

- Dentinsialophosphoprotein (DSPP) – marker for odonotoblast differentiation [2,3] and important for dentinogenesis and ECM mineralization [4].

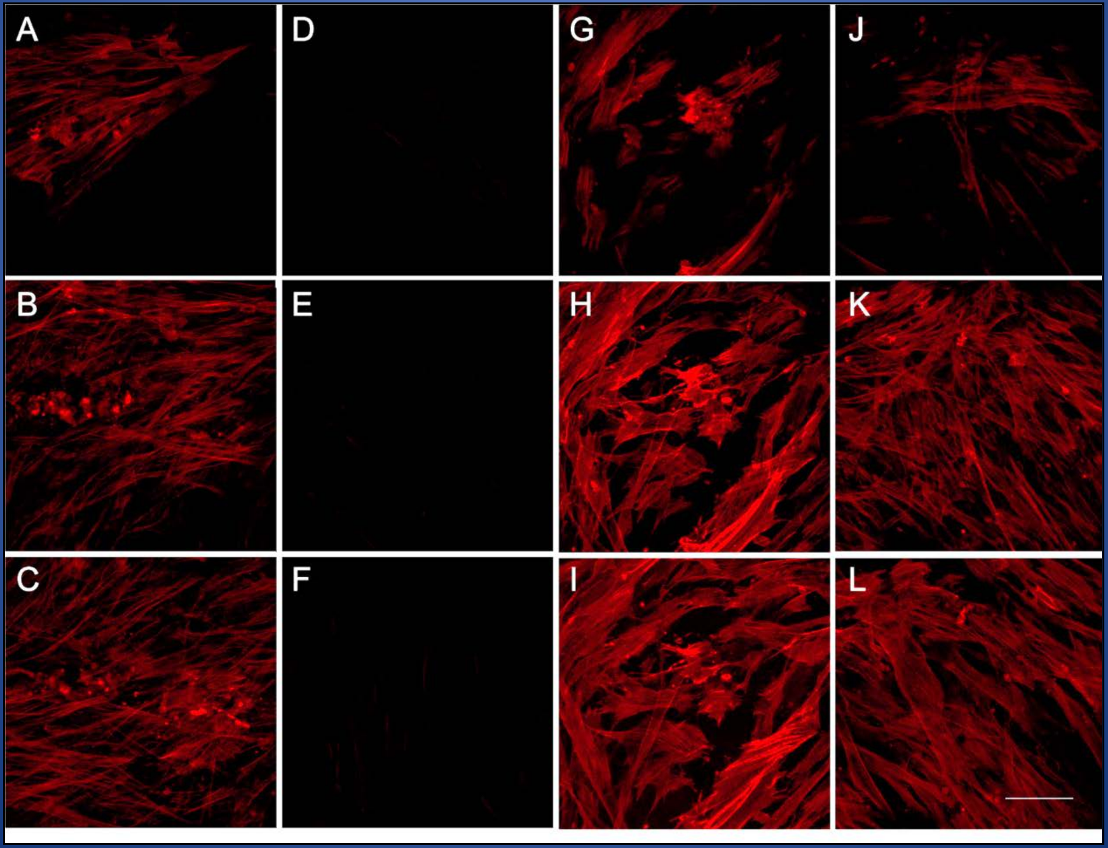
- Alkaline Phosphatase (ALP) – enzyme involved in tissue mineralization, is essential for deposition of minerals in bone and teeth

1. Rickard DJ, Sullivan TA, Shenker BJ, Leboy PS, Kazhdan I. Induction of rapid osteoblast differentiation in rat bone marrow stromal cell cultures by dexamethasone and BMP-2. Dev Biol 1994;161:218 –28.
2 Butler WT. Dentin specific proteins. Methods Enzymol 1987;145:290–303.
3 Butler WT, Brunn JC, Qin C, McKee MD. Extracellular matrix proteins and the dynamics of dentin formation. Connect Tissue Res 2002;43:301–7.
4 Yamada Y, Fujimoto A, Ito A, Yoshimi R, Ueda M. Cluster analysis and gene expression profiles: a cDNA microarray system-based comparison between human dental pulp stem cells (hDPSCs) and human mesenchymal stem cells (hMSCs) for tissue engineering cell therapy. Biomaterials 2006;27:3766–81.
5 Fujisawa R, Butler WT, Brunn JC, Zhou HY, Kuboki Y (1993).Differences in composition of cell-attachment sialoproteins between dentin and bone. J Dent Res 72:1222-1226.

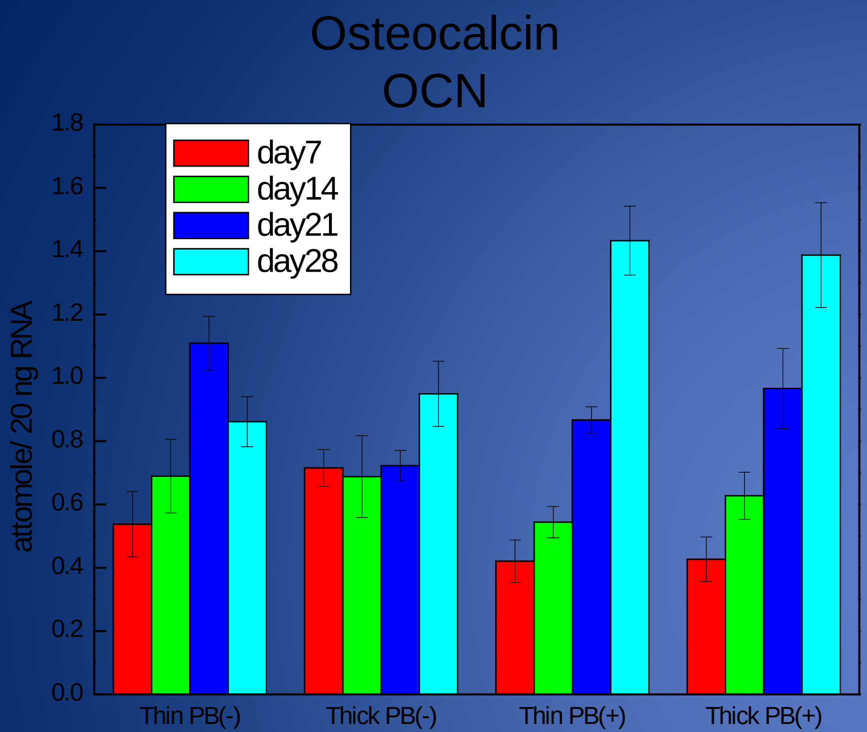
Dental pulp cells respond to surface mechanics:

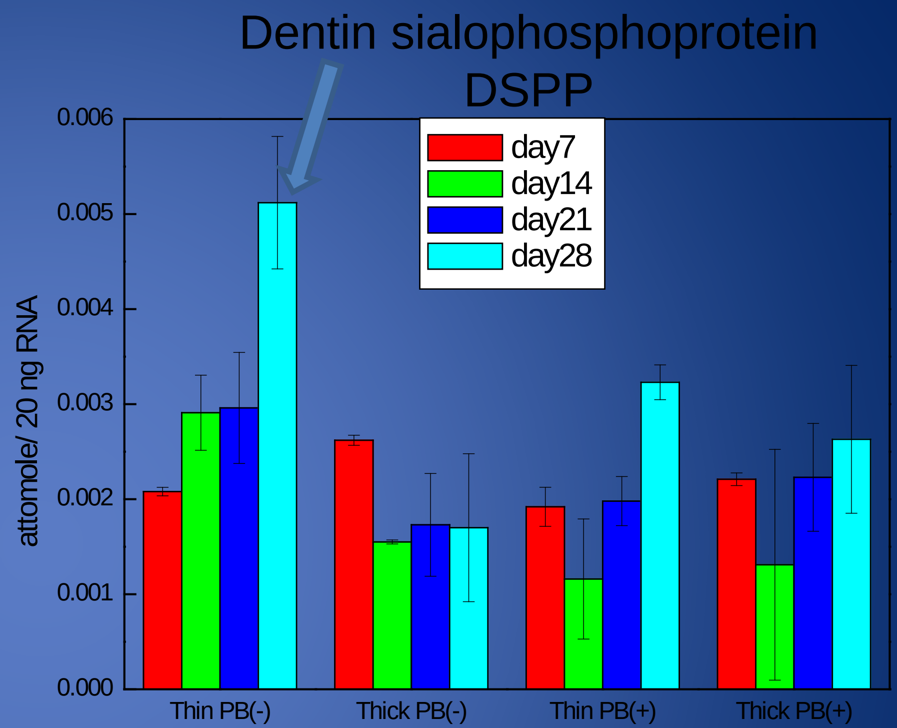
Mechanics controls osteocalcin expression (differentiation marker)

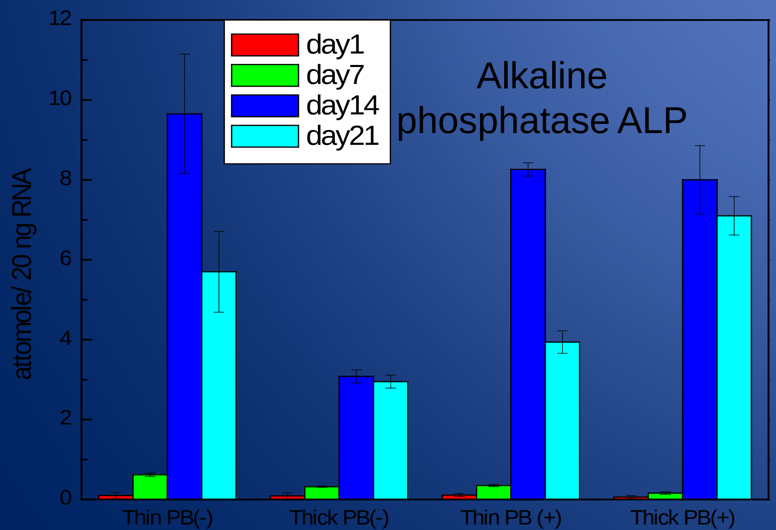
-Dex 200Å	-Dex 2000Å	+Dex 200Å	+Dex 2000Å



RT-PCR: Surface induced gene expression DPSCs







- ALP is elevated on all, except thick (-) PB.
- Dex induces **osteogenesis**; OCN high .
- Thin (-) PB induces **odontogenesis**

(OCN decreases while DSPP increases @ 28 d)

- Thick (-) PB: **No induction w/o dex.**

WHAT IS THE IMPACT OF MECHANICAL HETEROGENEITY?

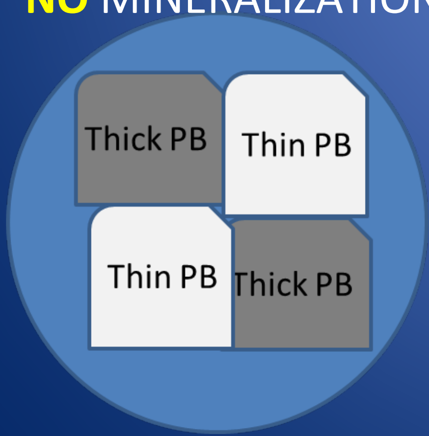
cm Length Scale Differences in Mechanics

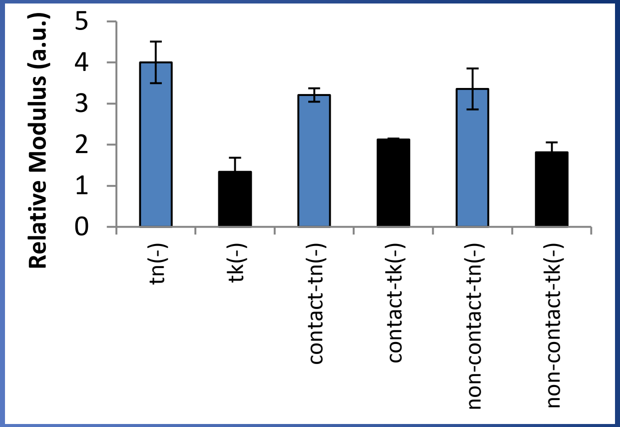
Soluble factors limit response to substrate mechanics

NO MINERALIZATION

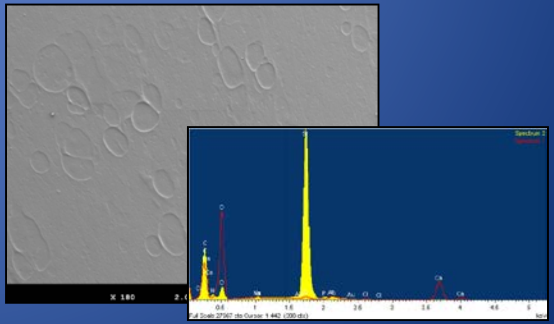
MINERALIZATION

NO MINERALIZATION





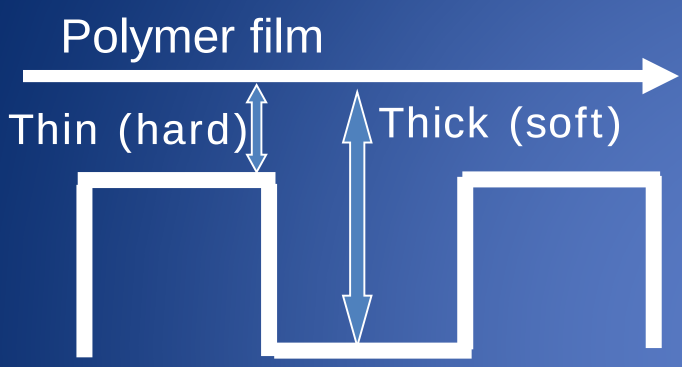
Cell moduli are responsive to substrate moduli , BUT



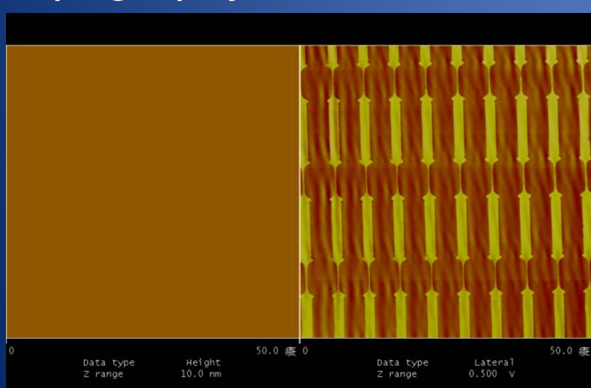
No mineralization on thin PB (-Dex) in co-culture with cells on thick PB

μm Length Scale differences in mechanics

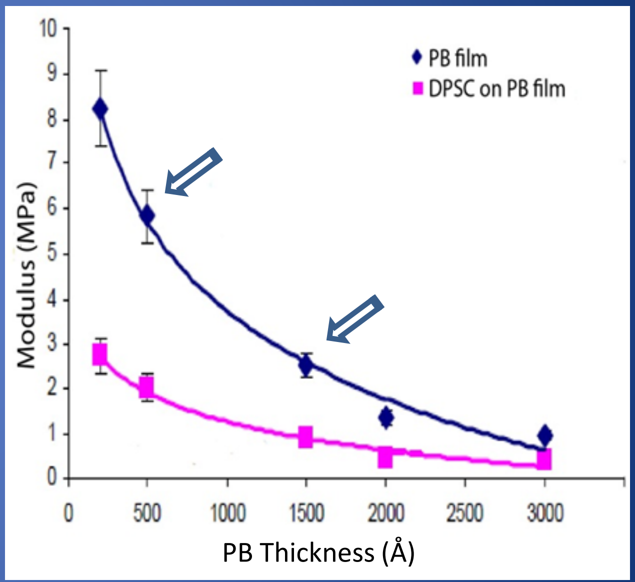
(Identical chemically and topographically)



Topography Lateral Force



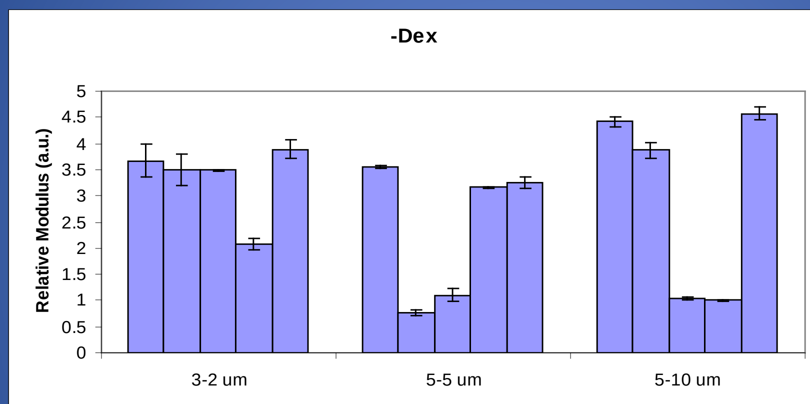
50μm

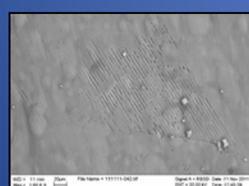


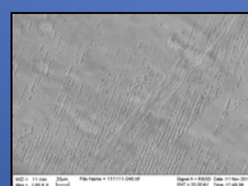
Pattern was produced by microlithography

PB was spun cast over the surface

For µm length scales:
Cell moduli follow surface moduli but mineralization does not
Soluble factors limit response to substrate mechanics



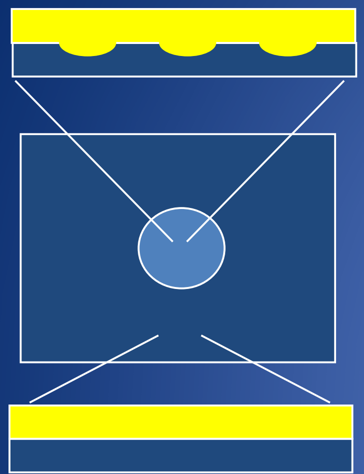




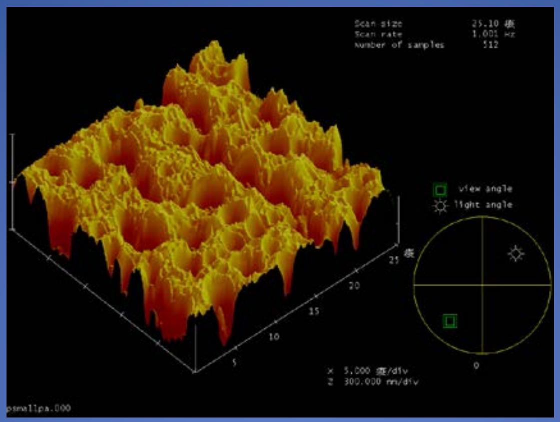
3-2 µm 5-5 µm 5-10 µm

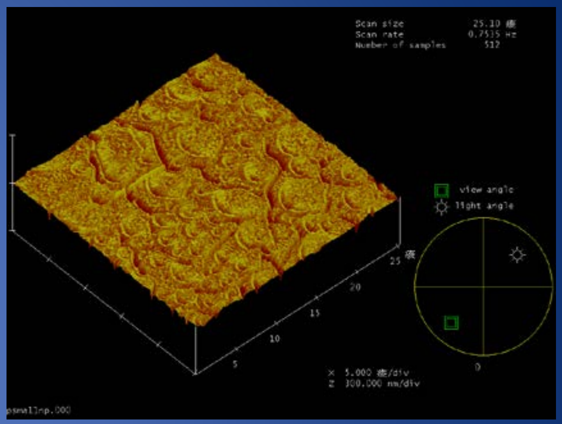
nm Length Scale: cells feel multiple stimuli

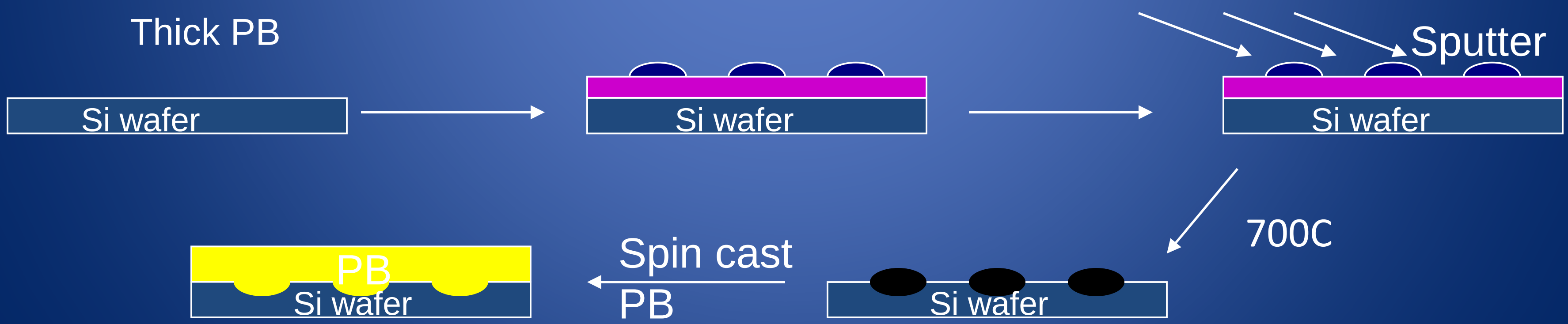
Patterned area



Non-patterned area







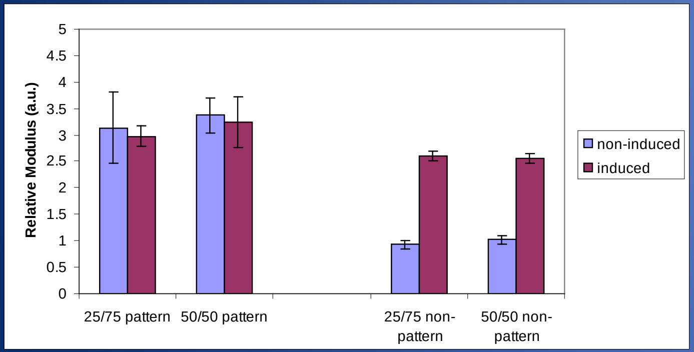
Nanopatterns were produced by imprinting from a phase separated polymer blend mask (PS/PMMA)

nm Length Scale Heterogeneity

Soluble factors do not limit cell responses to surface moduli

Cell moduli on patterns are high (d7)

Patterns   Thick PB

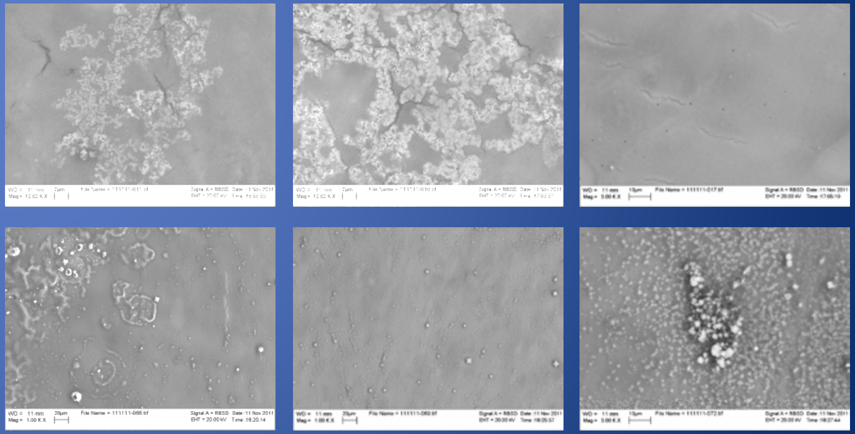


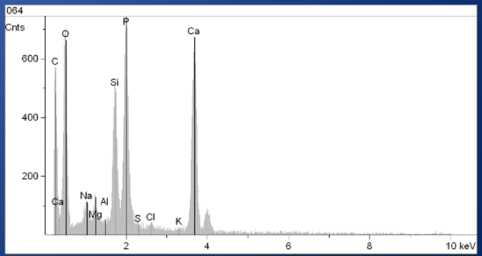
Mineralization on patterned surface does not require dexamethasone (d28)

25/75   50/50   thick PB

-Dex

+Dex





Length Scale: Regulation of Cell Function

When cells feel only one stimulus (cm to µm) -- soluble factors predominate

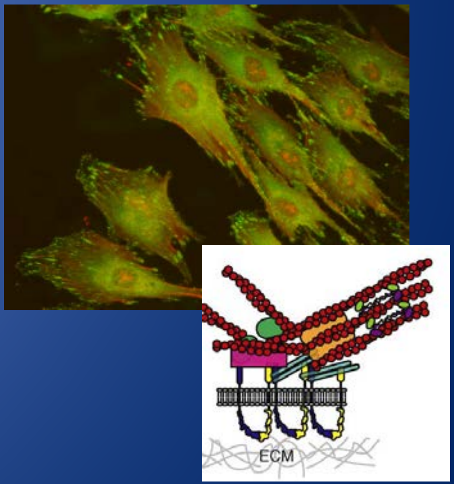
Disconnect between modulus and mineralization

When cells feel multiple stimuli (nm) -- direct cell:substrate interactions can override soluble factor effects

Increase in cell modulus and increase in mineralization

Focal Adhesions

- Signals from surface control cell mechanics and phenotype
- FA are as large as 1-5 µm with submicron to micron spacing



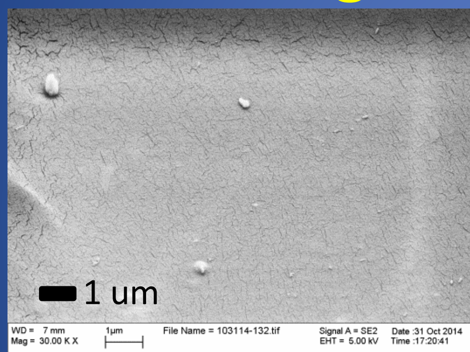
Choi et al, Trends Cell Bio 2010, 20(12)705

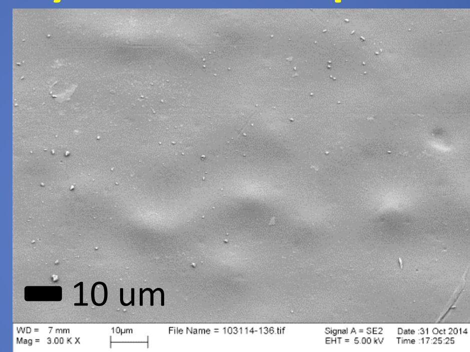
SEM of molded and 3D printed PLA

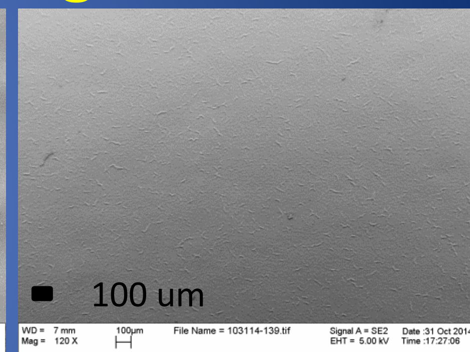
(Makerbot Replicator™ 2X, PLA filament)

Heterogeneity at multiple length scales

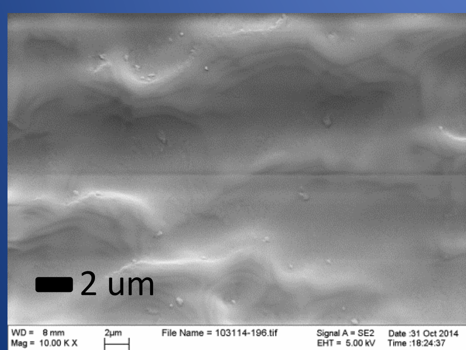
Molded

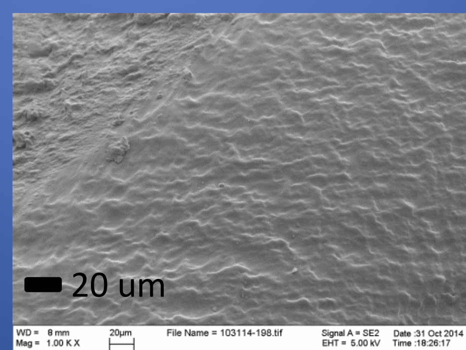


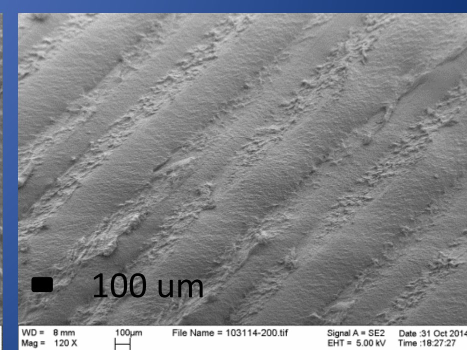


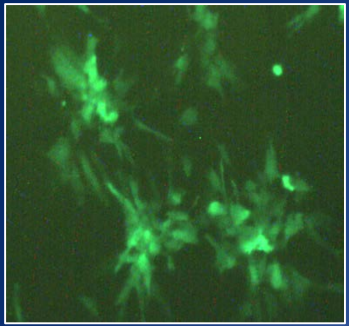


3D Printed



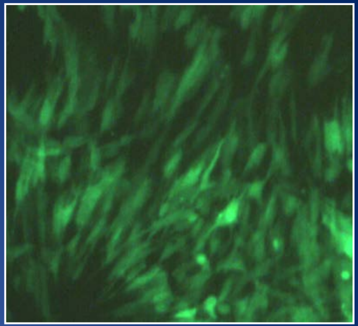




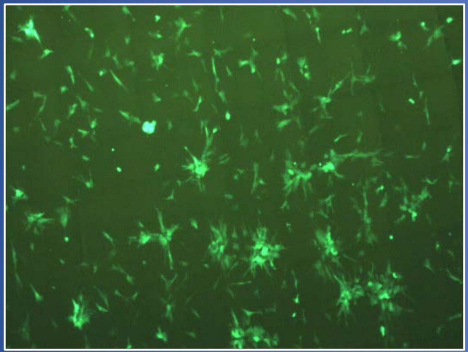


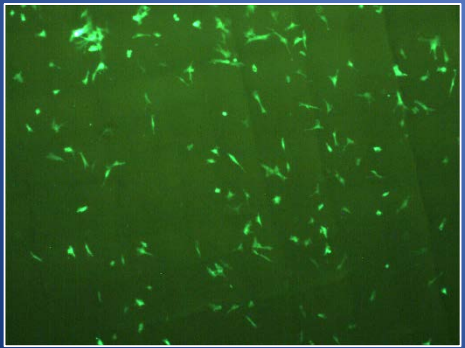
DPSC – plated on non-sterilized PLA

(24 hours post-plating)

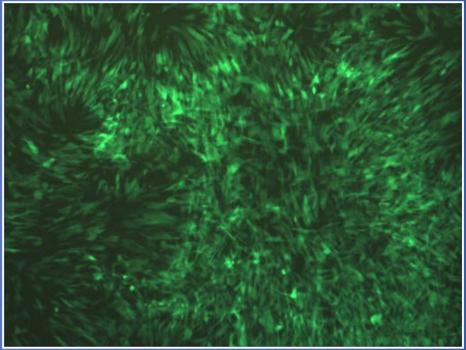


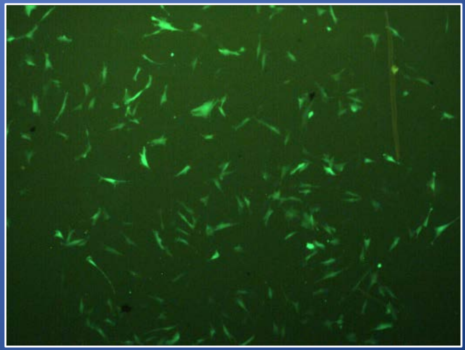
3D Printed



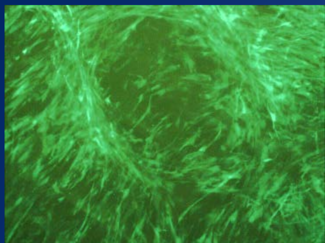


Molded



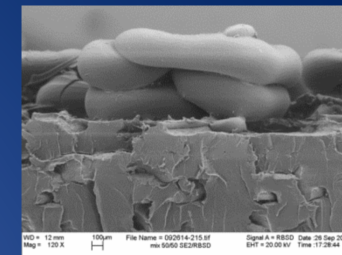


Day 28/3D



Adhesion and Proliferation

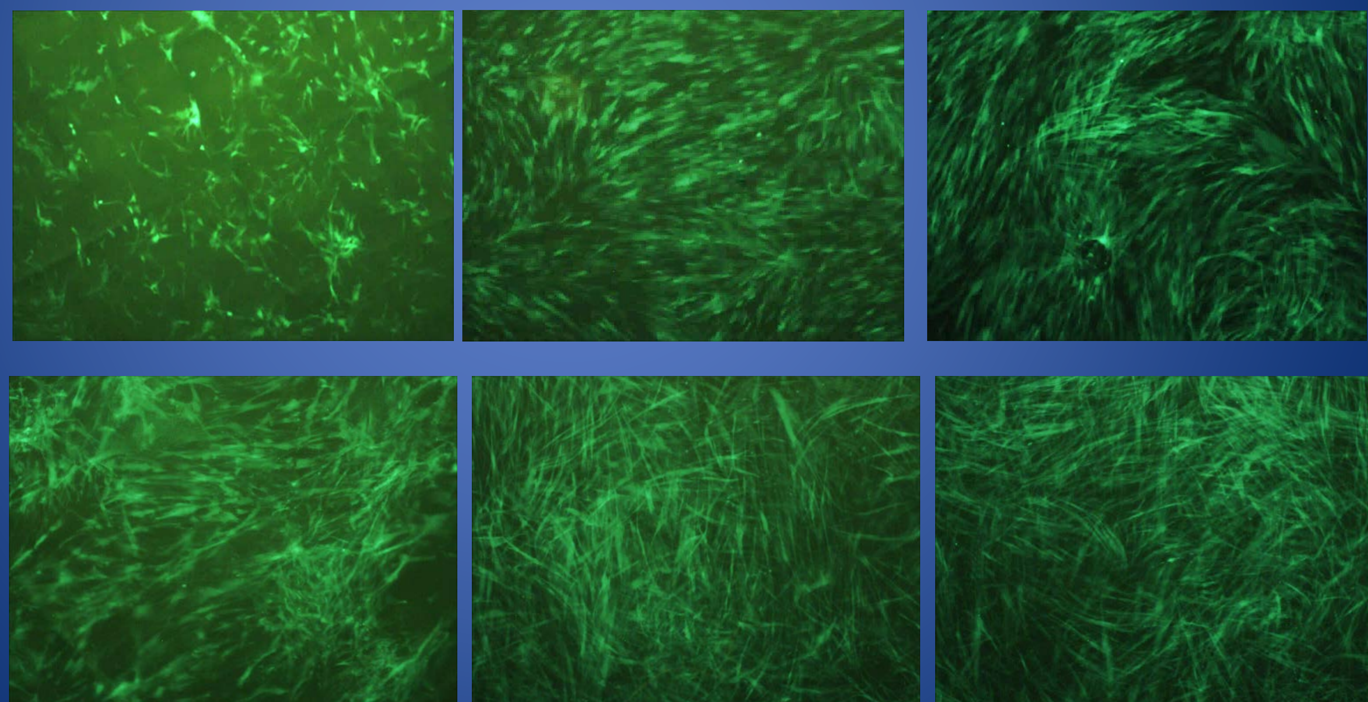
Topography Vs Ethylene oxide sterilization



3D | Molded | Tissue Culture Plastic

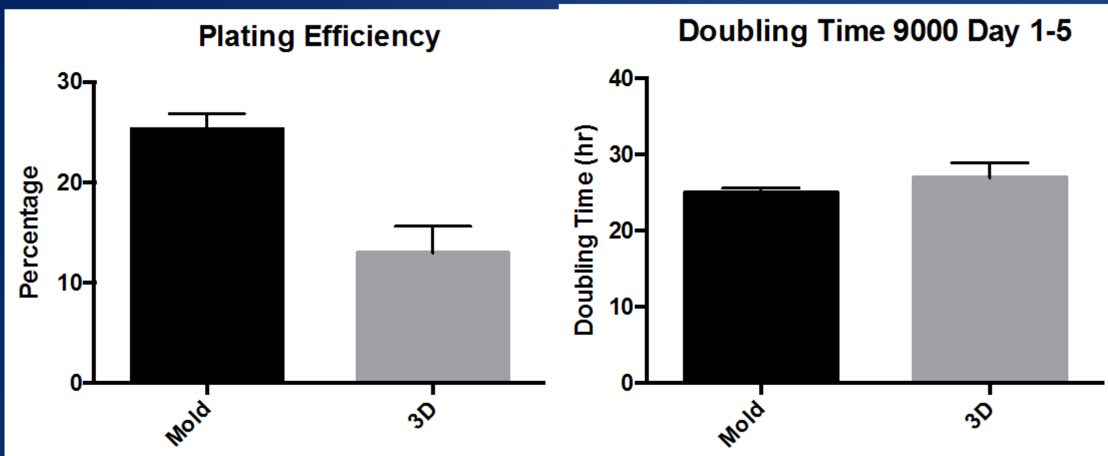
Day 1

Day 13

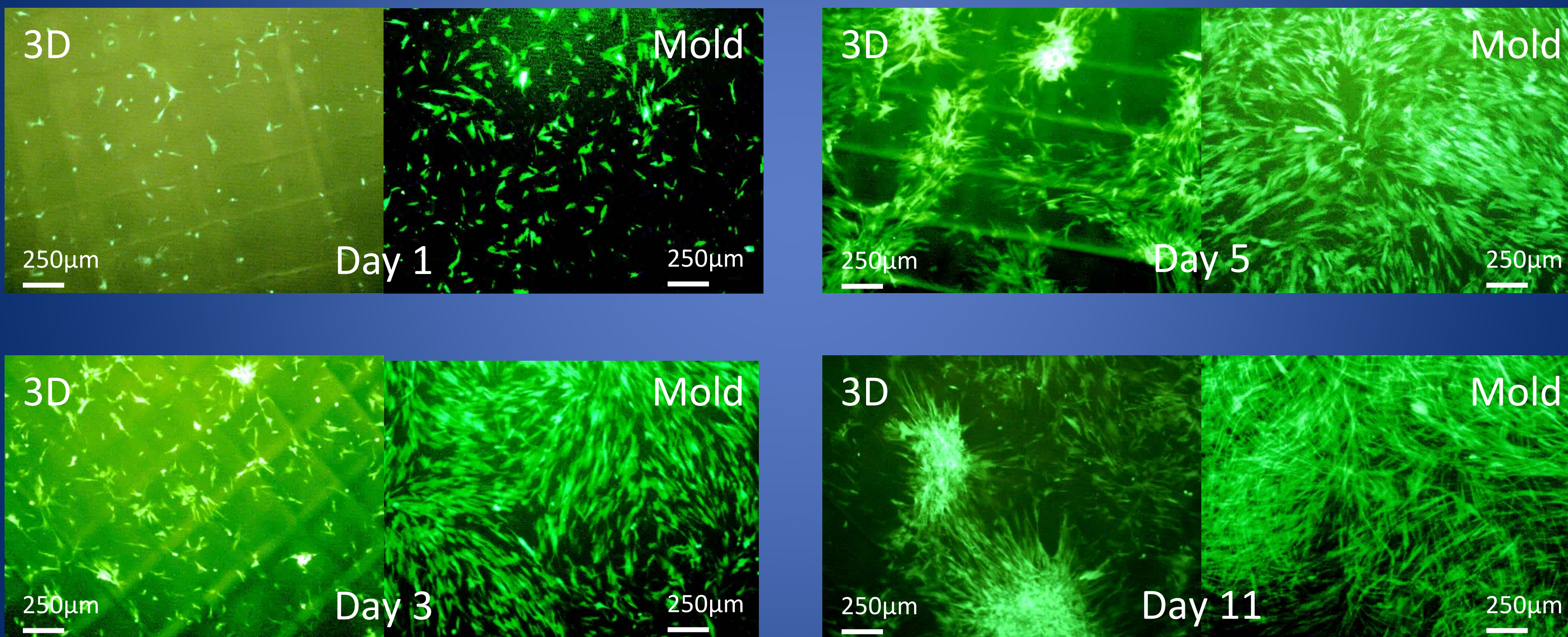


Ethylene oxide: representative pictures (n=3)

Fluorescent Microscopy

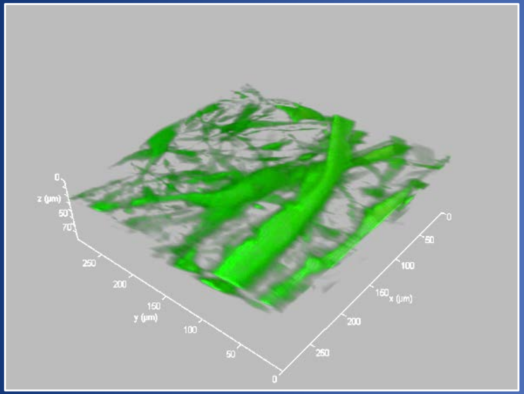


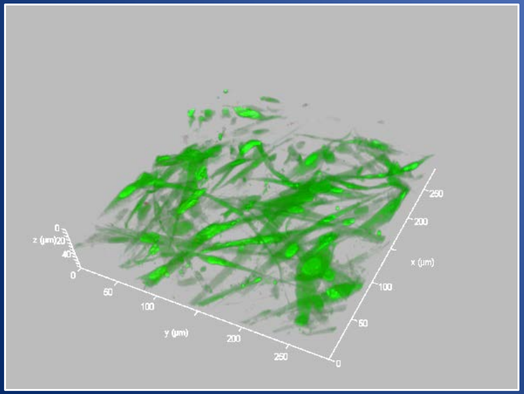
Plating density 9000/cm^2



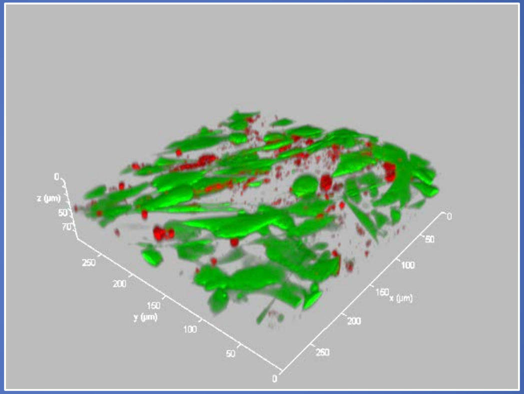
Cells and mineral deposits (28 d)

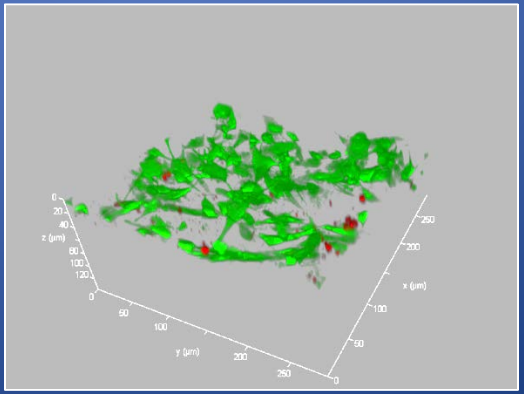
Molded



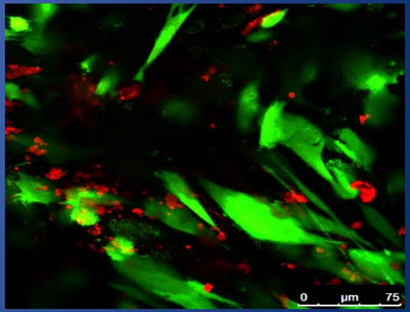


3D Printed





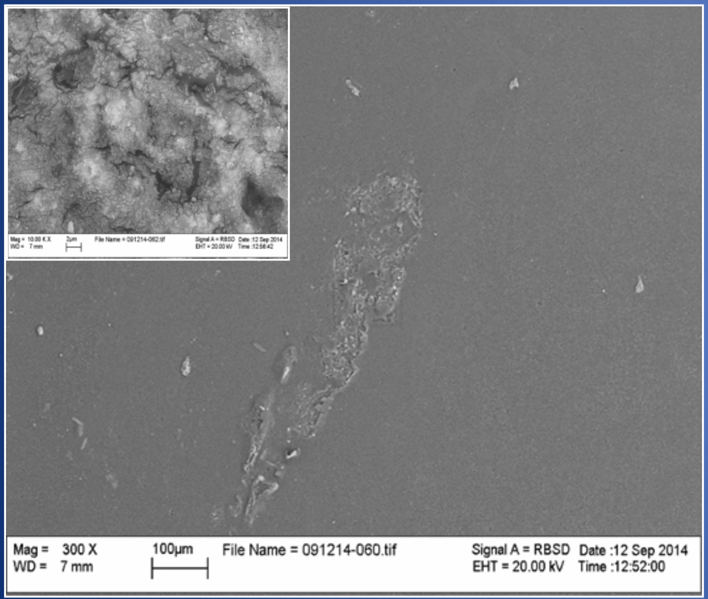
- Dexamethasone

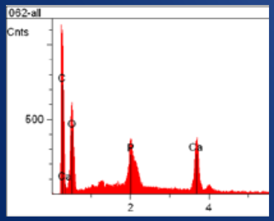


+ Dexamethasone

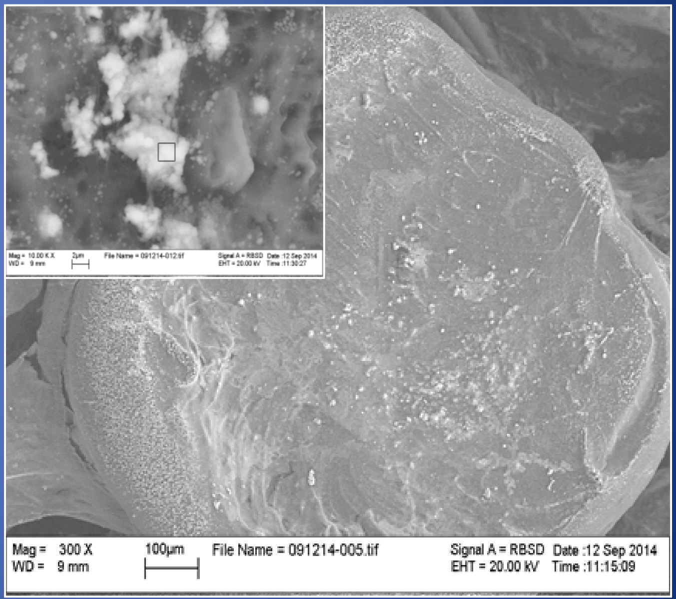
Calcium phosphate: SEM/EDX

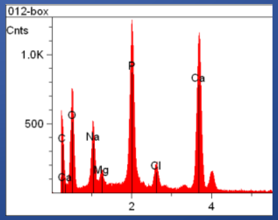
Molded





3D Printed
(High resolution)

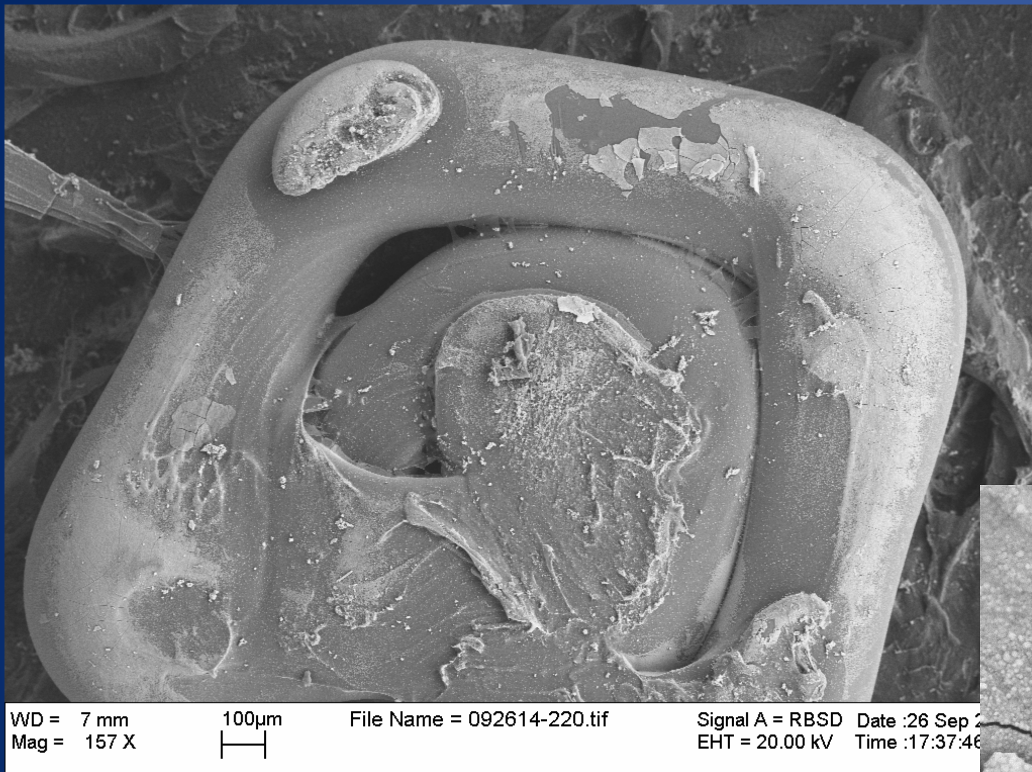


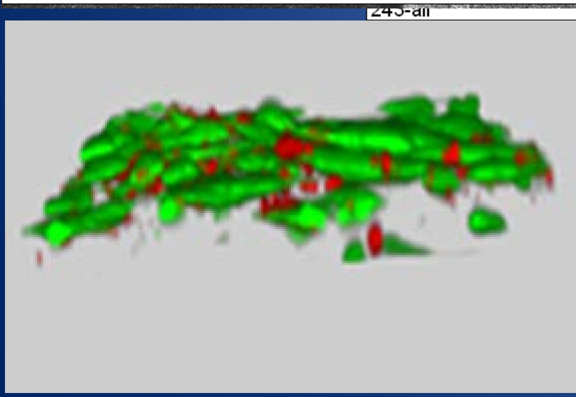


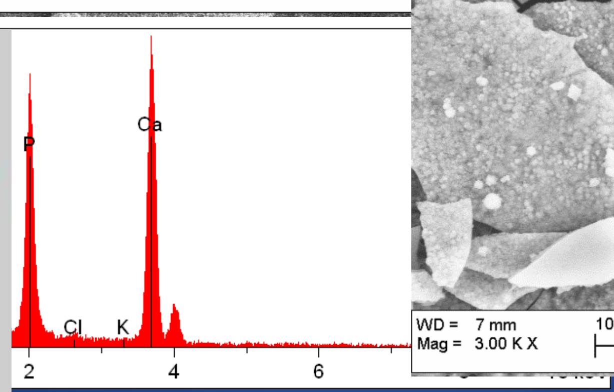
(- Dexamethasone)

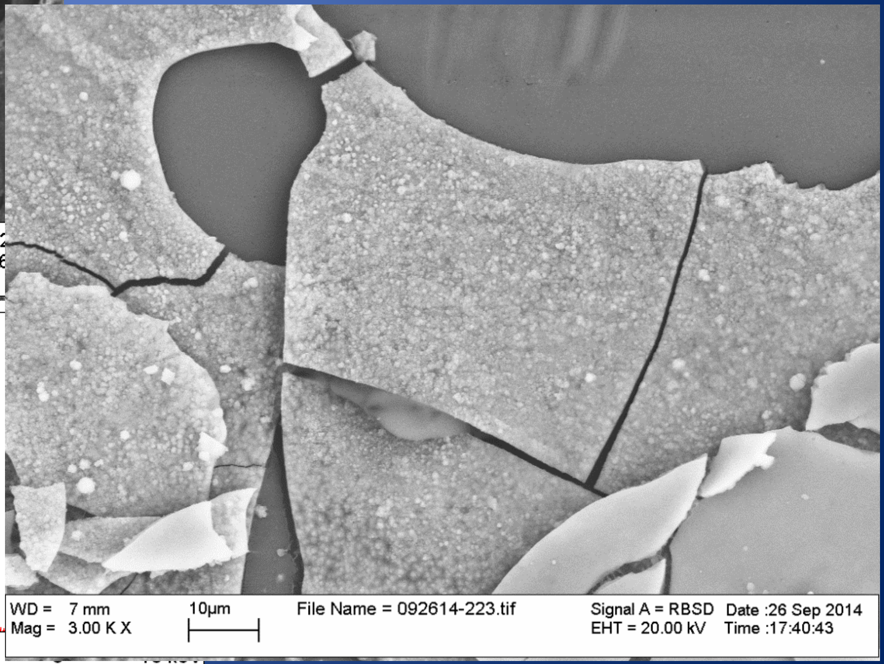
PLA: Standard resolution -DEX

- Microns thick biomineralized layer.
- Nanoscale roughness induces cell differentiation.
- Flat and rough surface together—Boiomineraliztion overides micro-roughness in co-culture

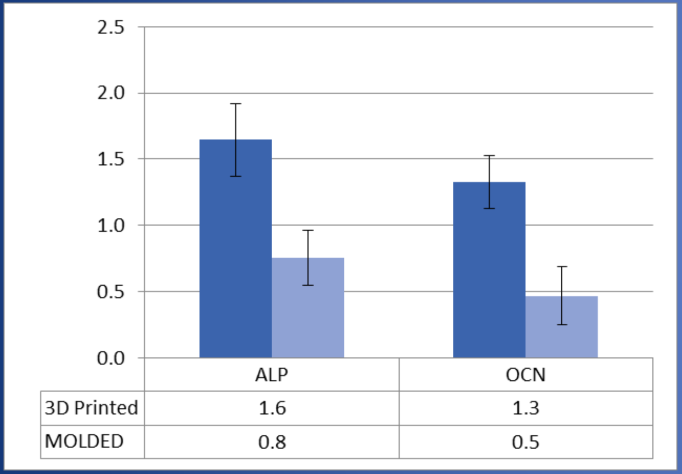








Differentiation (RNA markers)

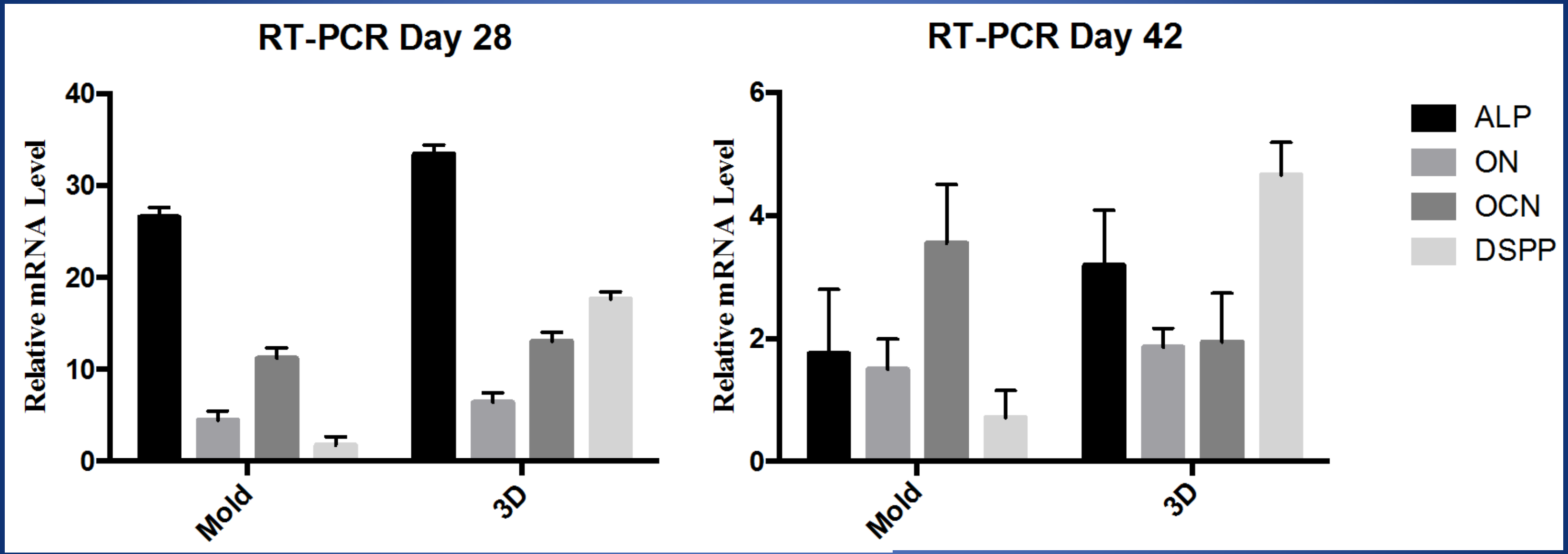


qRT-PCR

-Cells grown for 28 days (-dexamethasone)
-mRNA isolated
-cDNA prepared
-qPCR carried out with primers against alkaline phosphatase and osteocalcin

18S RNA was used to normalize RNA levels
Data shown is relative to β-glycerol phosphate negative control (TCP)

RT-PCR



The surface induced odontogenic differentiation in the Absence of another cytokines.

Conclusion

Cells respond to nanoscale surface structure.
AM surfaces have roughness on multiple scales due multiple factors

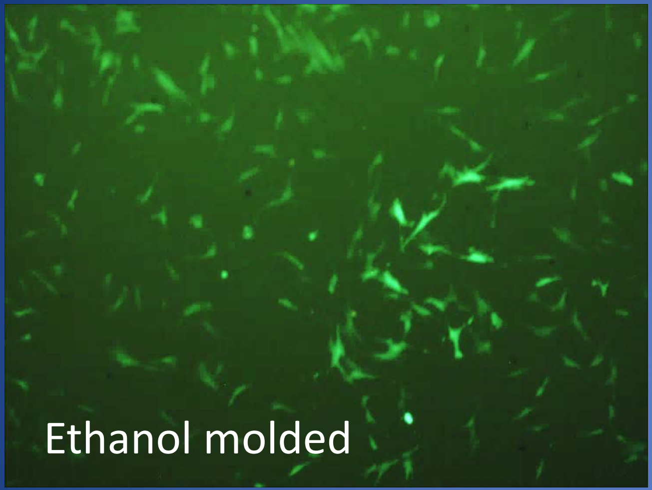
To move AM forward we must have a better understanding of the underlying science.

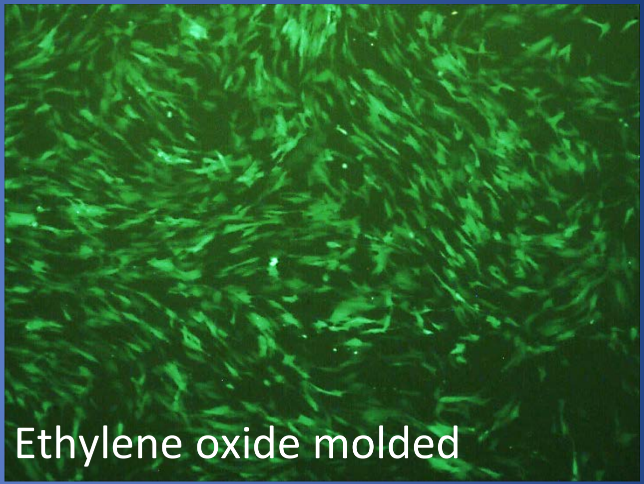
In-Situ Characterization of the polymer being printed makes this possible.

THANK YOU

This work was supported in part by NSF-Inspire award #1344267 and NYSTEM award #CO28096

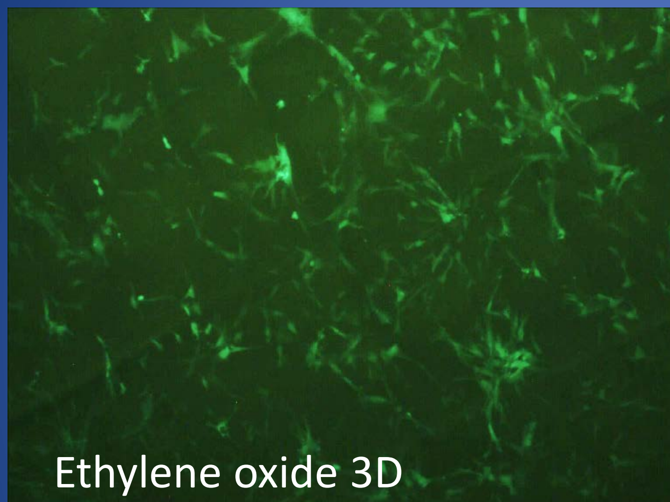
Day 1 post plating: Ethanol Vs Ethylene oxide





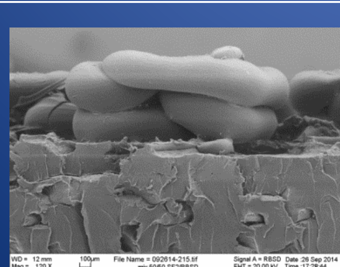
Day 1 post plating

Reduced cell plating efficiency on 3D printed surface



Is there residual ethylene oxide
Or
Is topography impacting cell plating

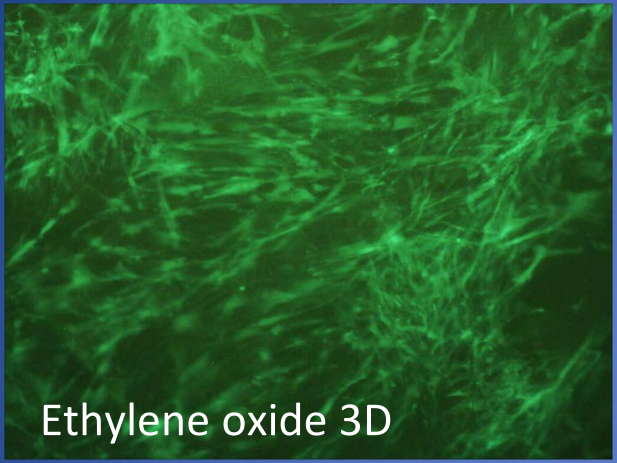
?

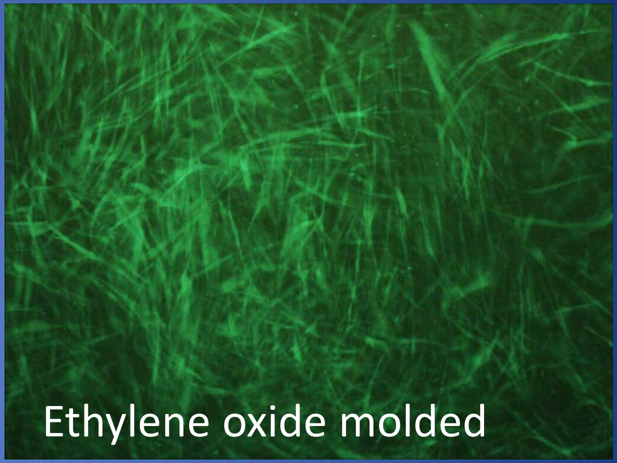


2/18/2015 experiment

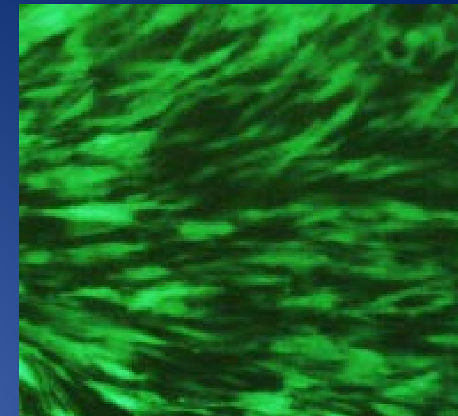
13 Days post plating

Cells on 3D printed surface proliferate





Cell morphology

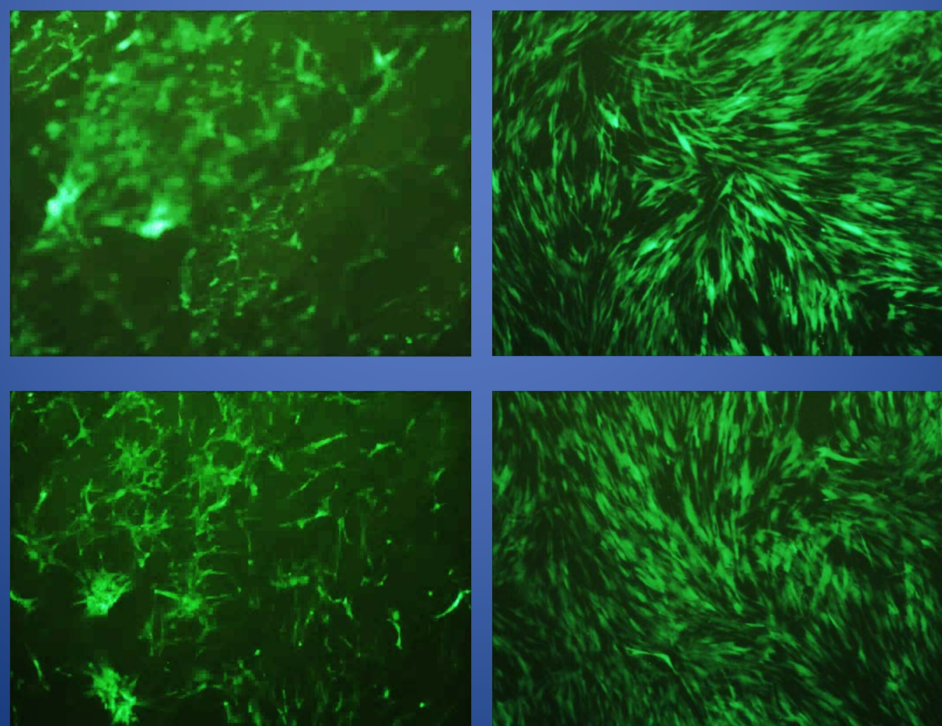


DAY 7 POST-PLATING

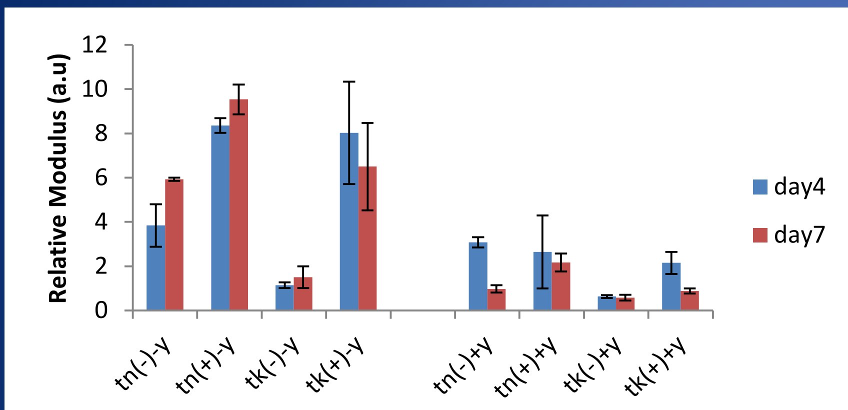
3D printed (HR) | Molded

Ethanol

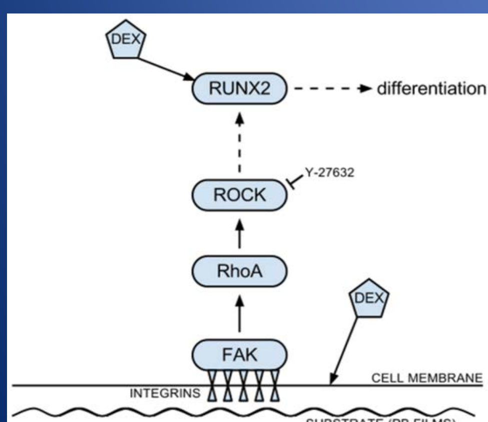
Ethylene oxide



Focal Adhesions:
ROCK inhibition decreases cell moduli and mineralization



Inhibition of ROCK reduces cell moduli



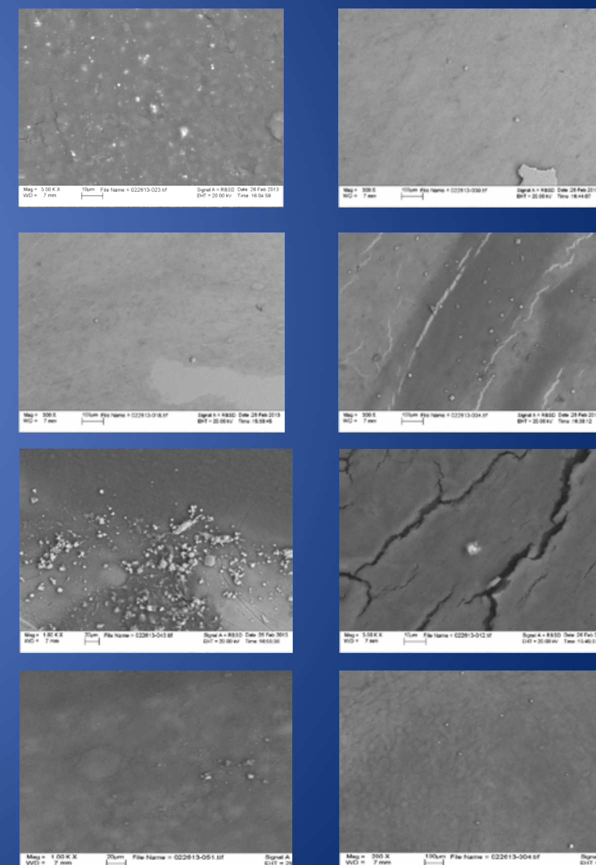
-Y2732 | +Y2732

-Dex, Thin

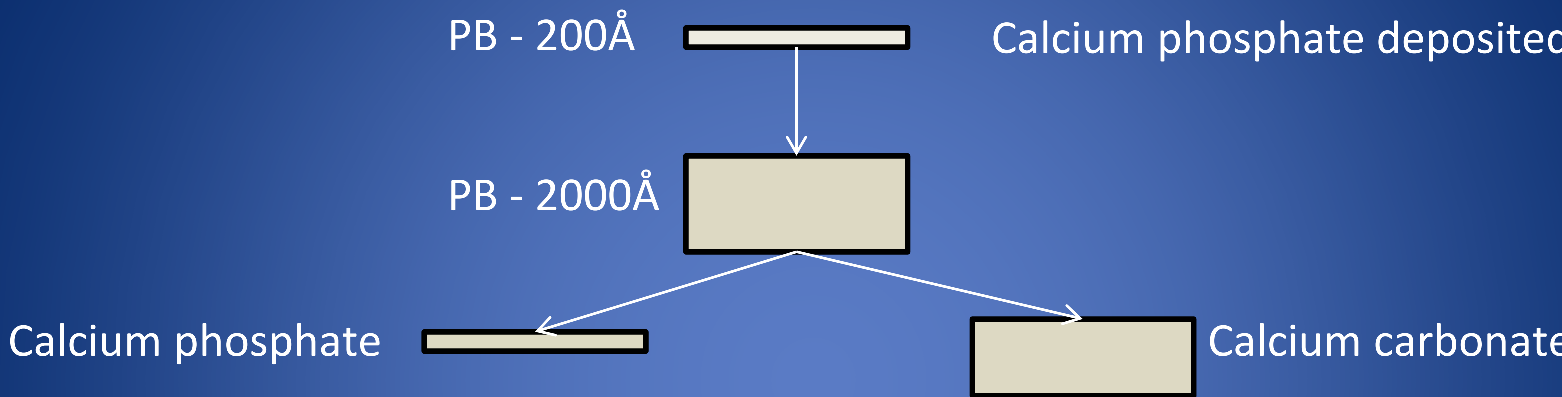
-Dex Thick

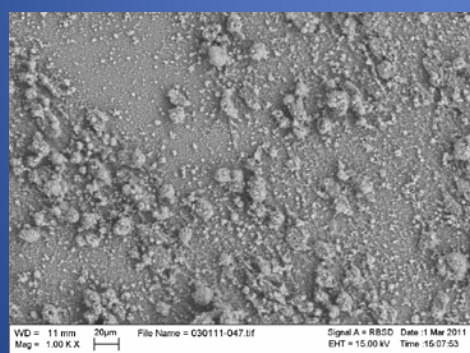
+Dex Thin

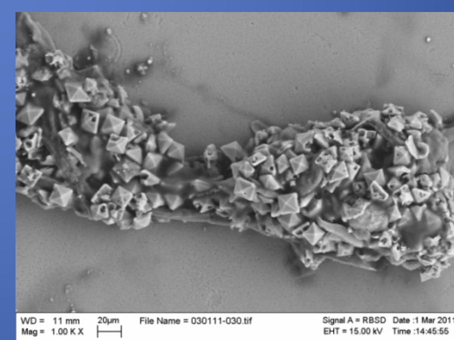
+Dex Thick

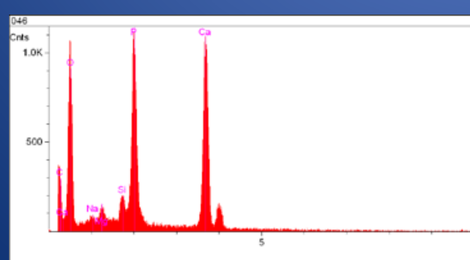


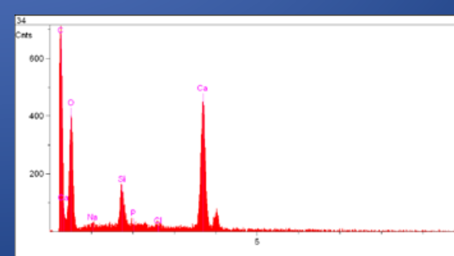
Is surface-induced phenotype reversible?
(Growth on PB without dexamethasone)







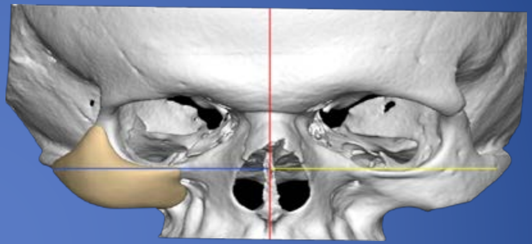


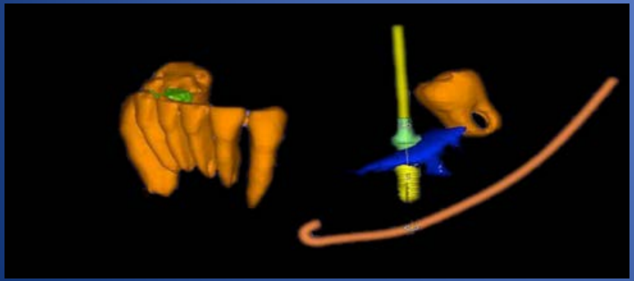


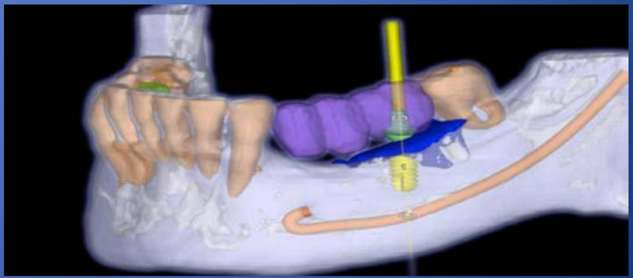
Additive Manufacturing of Bone Grafts

Repair of ameloblastoma

Repair of traumatic injury







Required to stabilize implants

Images: Courtesy of M Abboud

Cartilage replacement with porosity for cell penetration

The Wake Forest Institute for Regenerative Medicine prints ear, nose and bone scaffolds that can be coated with cells to grow body parts. (Laurie Rubin)

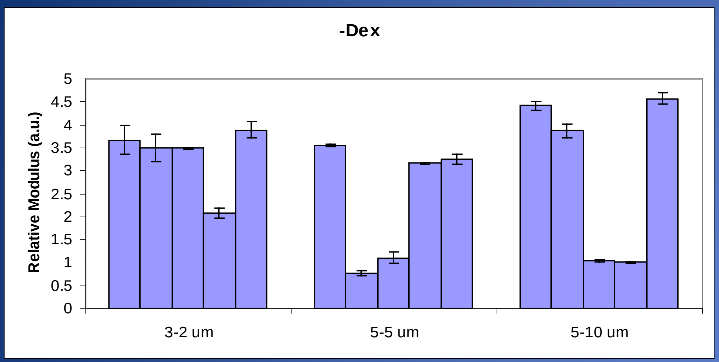
Fabrication of PGA/PLA Scaffold With the Shape of Human Nose http://dx.doi.org/10.5772/55540

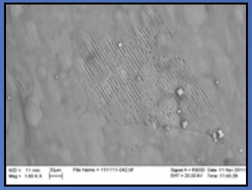
Will cells respond similarly to printed and molded forms?

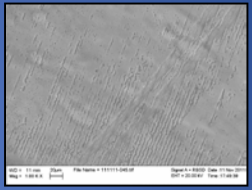
TO QUESTIONS FACING MEDICINE TODAY:

TO WHAT EXTENT ARE 3-D PRINTED DEVICES EQUIVALENT TO TRADITIONAL MOLDED OR CAST ONES?

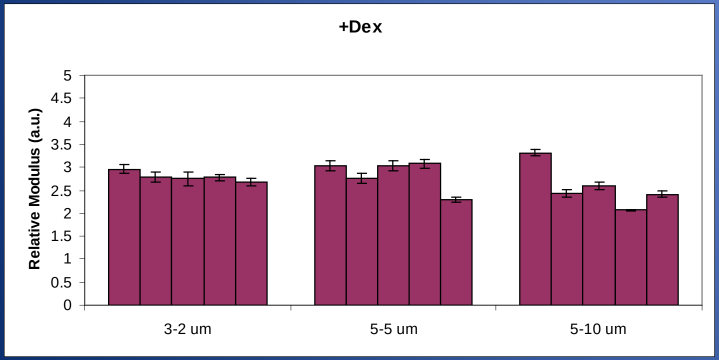
For µm length scales:
Cell moduli follow surface moduli but mineralization does not
Soluble factors limit response to substrate mechanics

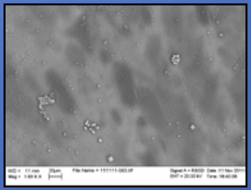


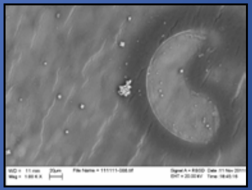


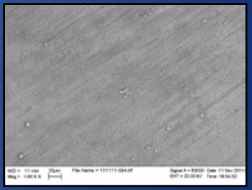


3-2 µm 5-5 µm 5-10 µm









3-2 µm 5-5 µm 5-10 µm