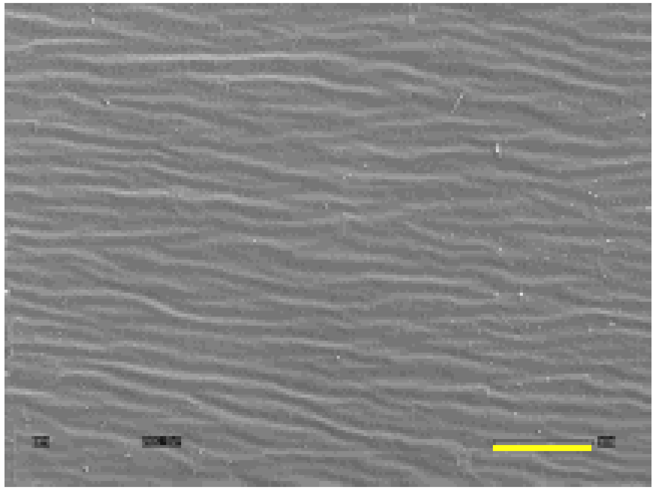
Polymer Surface Feature Dimension Reduction

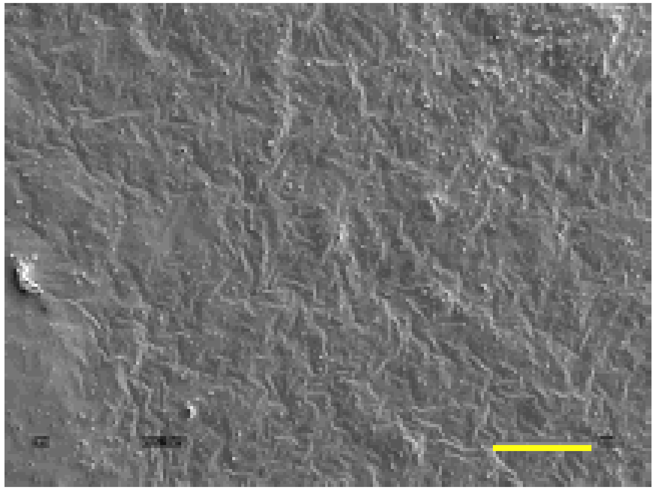
Polymer	Chemical Treatment	Treatment Time	Resulting Surface-Feature Dimension
PLGA	Untreated	None	Conventional (control)
	0.1 N NaOH	10 min	Small- micron
	5 N NaOH	30 min	Sub- micron
	10 N NaOH	1 hr	Nanometer
PU	Untreated	None	Conventional (control)
	0.1 N HNO_3	10 min	Sub- micron
	10 N HNO_3	30 min	Nanometer
PCL	Untreated	None	Conventional (control)
	0.1 N NaOH	1 min	Sub- micron
	0.1 N NaOH	10 min	Nanometer

Nano-structured PLGA Increases Vascular Tissue Regeneration

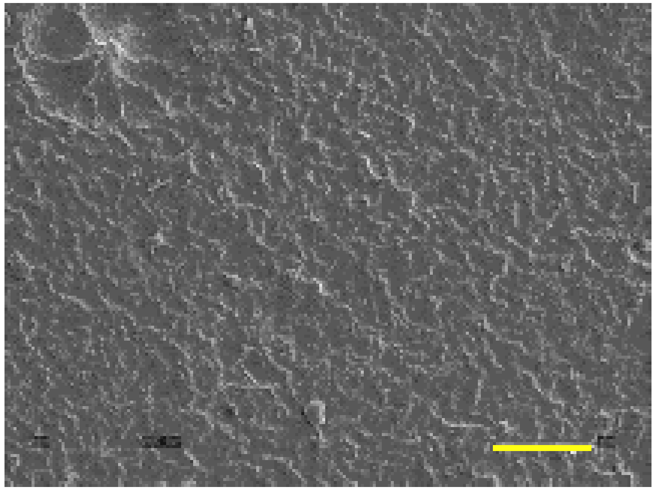


Control (Untreated)

Bar = 100 μm

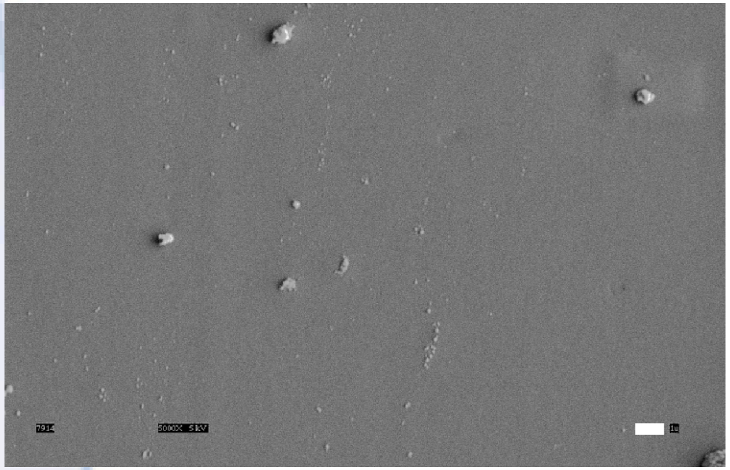


Sub-micron Structured



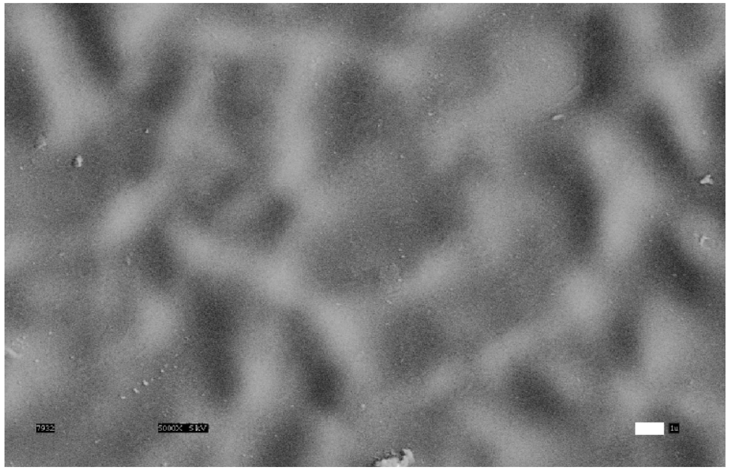
Nano-structured

Nano-structured PU Increases Vascular Tissue Regeneration

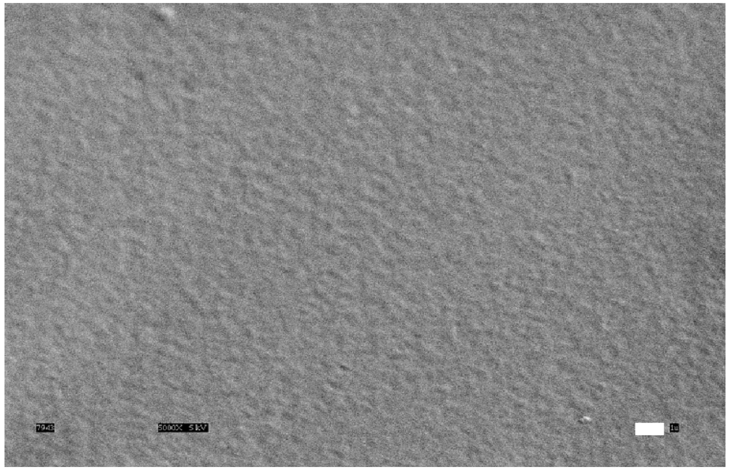


Control (Untreated)

Bar = 1 μm

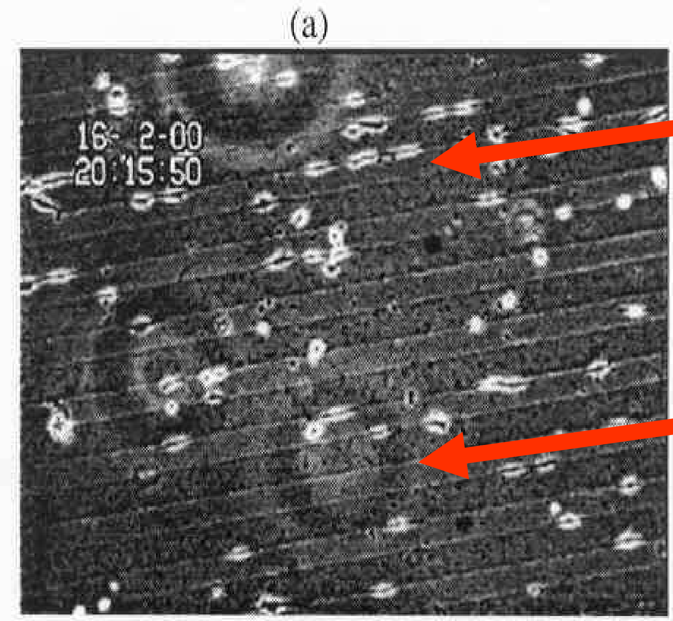


Sub-micron Structured



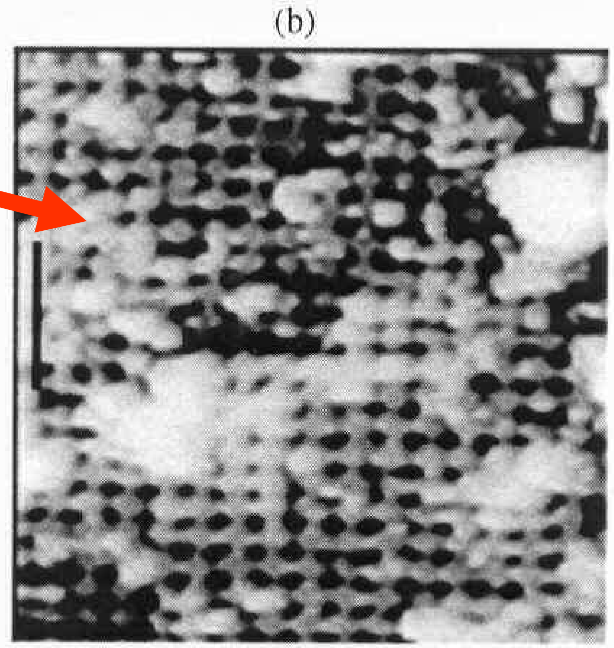
Nano-structured

Other Novel Nanopolymers



Aligned Endothelial Cells

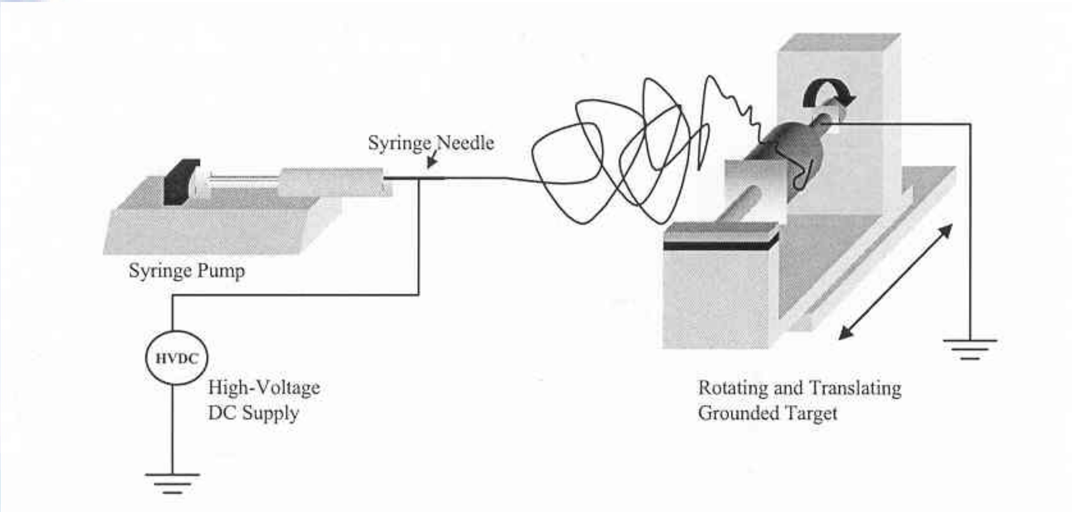
Aligned Nanostructured Grooves

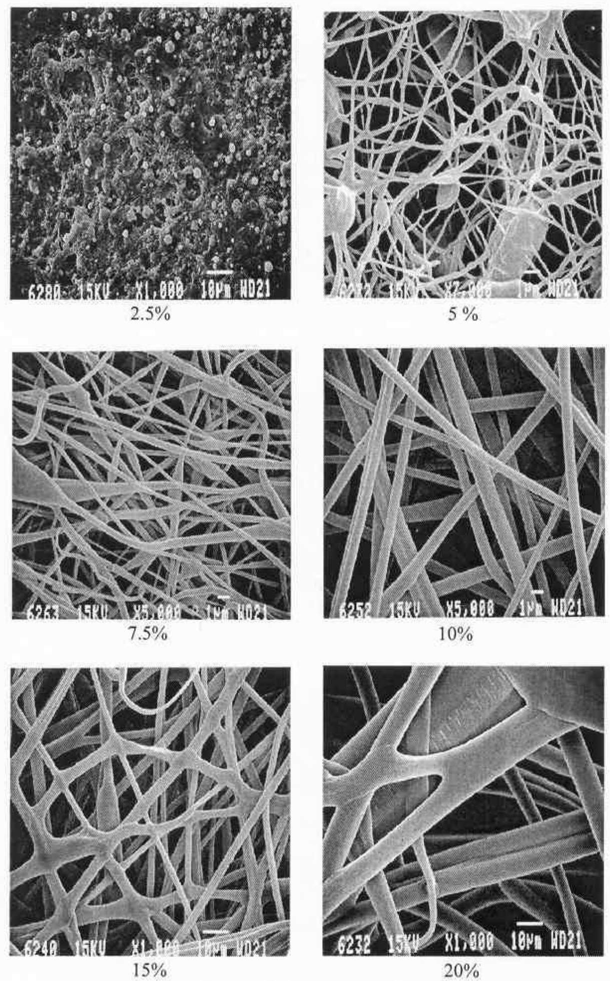


Increased Endothelial Cell Adhesion to Nano-structured Features Synthesized By Casting Polycaprolactone from Silica Molds

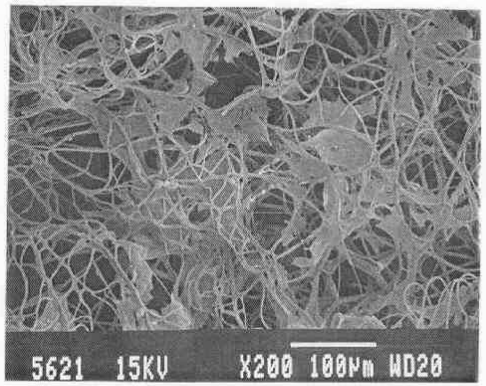
Curtis et al., Biophysical Chemistry 94 (2001): 275-283.

Other Novel Nanopolymers





Increased Functions of Smooth Muscle Cells on EVOH Nanofibers



Kenawy et al., Biomaterials 24 (2003):907-913.

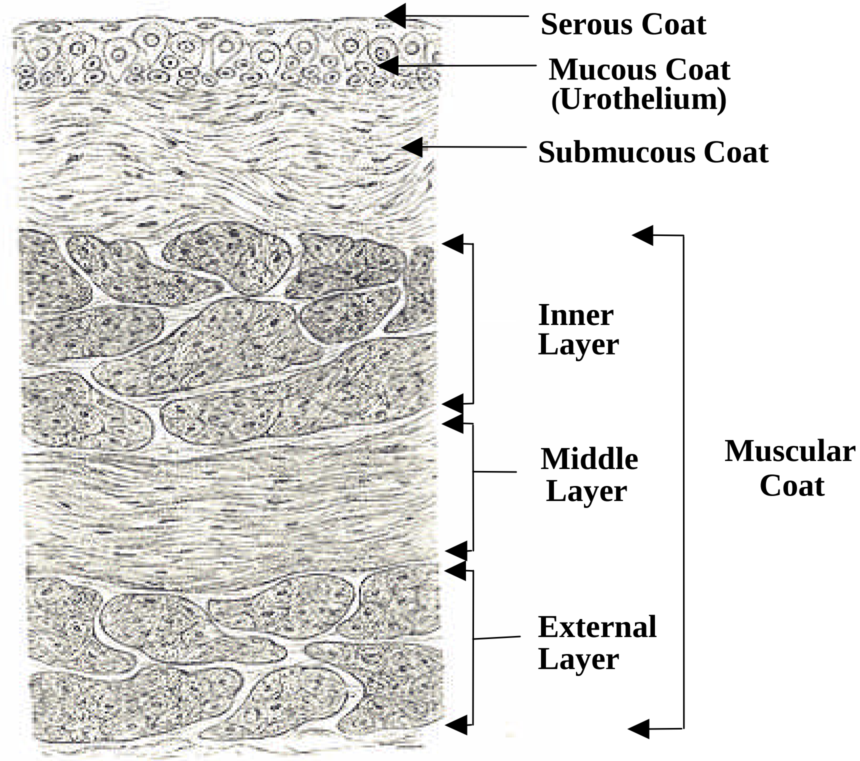
PART IV
Bladder: Nanostructured Polymers

The Problem:
Current Bladder Implant Failures

- 400 million people worldwide reportedly suffer from bladder disease (by 1999).
- Urinary bladder cancer is the most prevalent of these cases, and is the:
  - second most common malignancy of the genitourinary tract in the US; and
  - fourth leading cause of cancer among American men.
- 75-85% of bladder cancers are superficial and require cystectomy of the entire bladder.
- Therefore, there is a need for bladder tissue replacement constructs with increased efficacy.

Bladder Tissue: Another Nano-structured Tissue

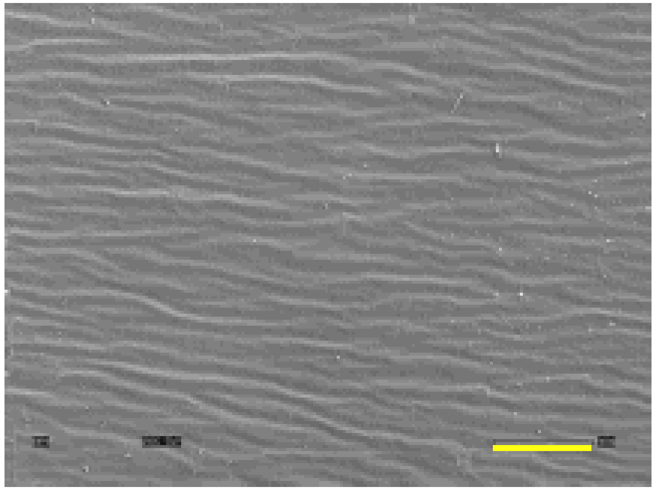
- 6- to 8-cell layer of transitional epithelium
  - Urothelial cells, ECM proteins
  - Inner lining of mucosal layer
- Loosely arranged submucosa
  - Acellular
  - Provides mobility to mucosa
- 3 layers of smooth muscle fibers
  - Smooth muscle cells, ECM proteins
  - External layer (longitudinal)
  - Middle (circular)
  - Inner layer (longitudinal)
  - Major portion of bladder wall



Schematic Diagram Depicting a Vertical Section of the Bladder Wall

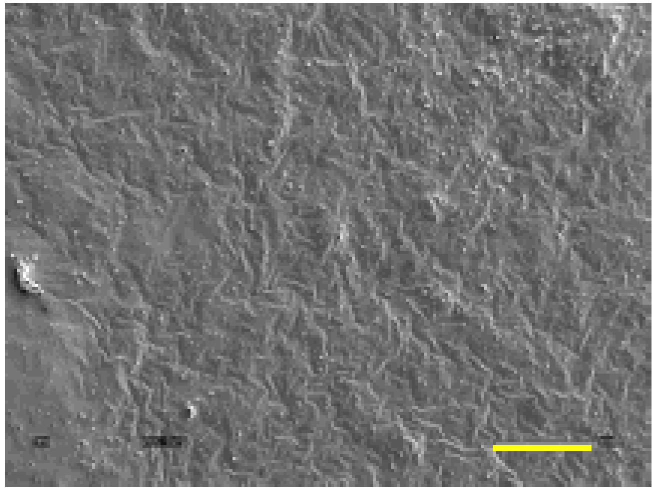
Source: Gray, Henry. *Anatomy of the Human Body*. Philadelphia: Lea & Febiger, 1918; Bartleby.com, 2000. www.bartleby.com/107/.

Nano-structured PLGA Increases Bladder Tissue Regeneration

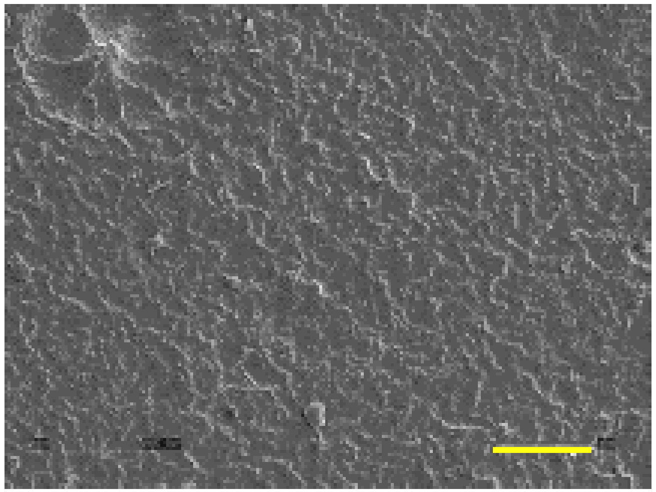


Control (Untreated)

Bar = 100 μm

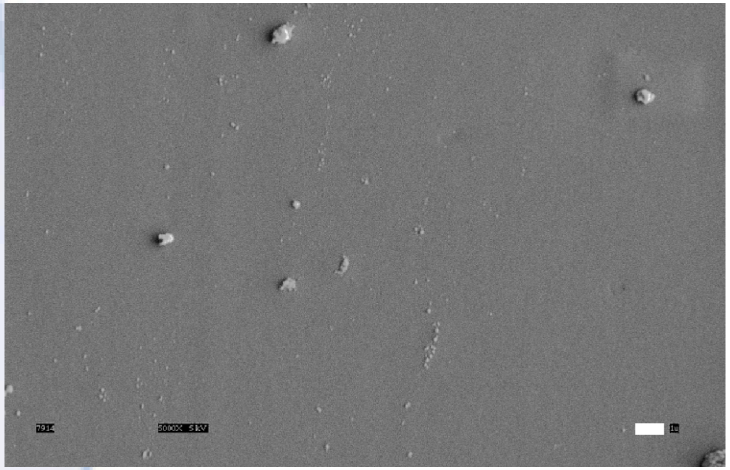


Sub-micron Structured



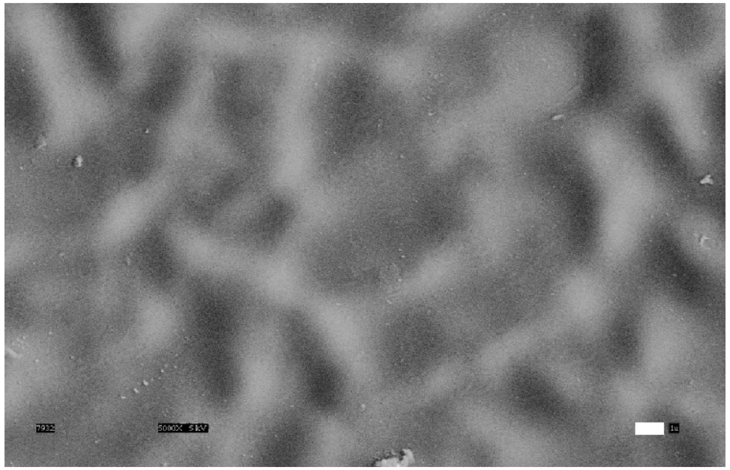
Nano-structured

Nano-structured PU Increases Bladder Tissue Regeneration

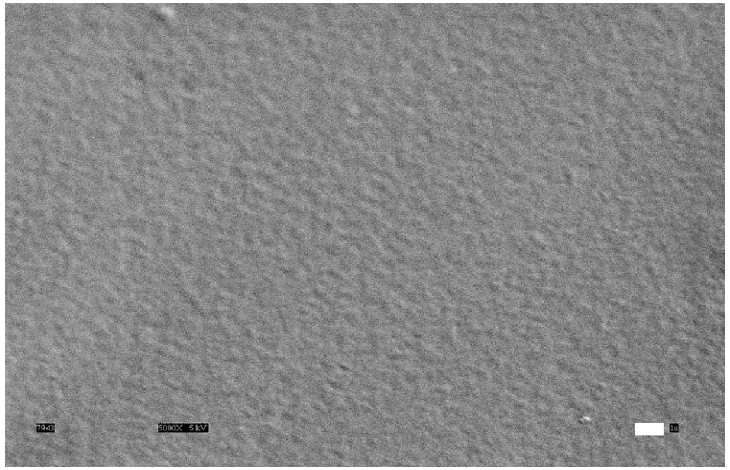


Control (Untreated)

Bar = 1 μm

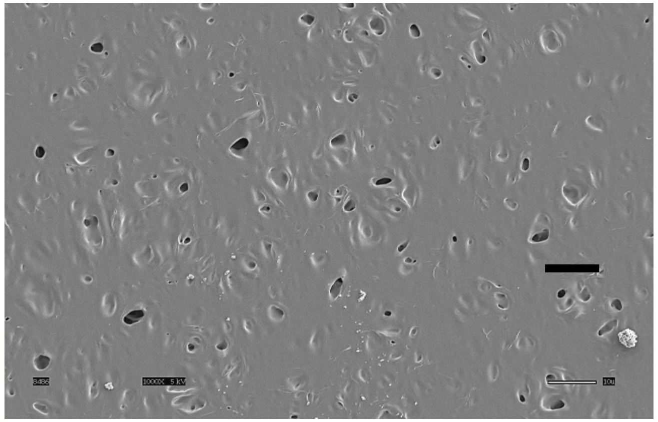


Sub-micron Structured



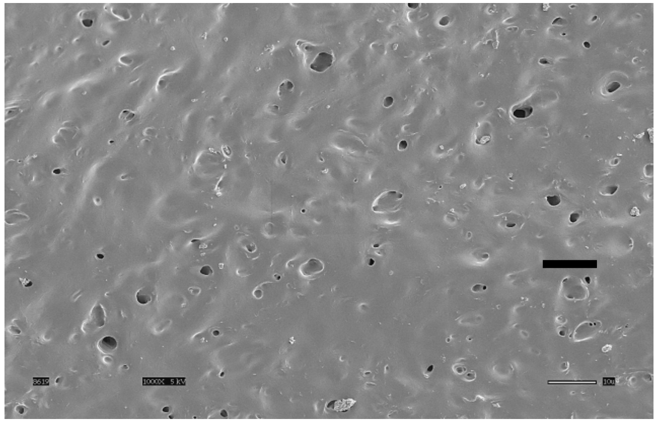
Nano-structured

Nano-structured PCL Increases Bladder Tissue Regeneration

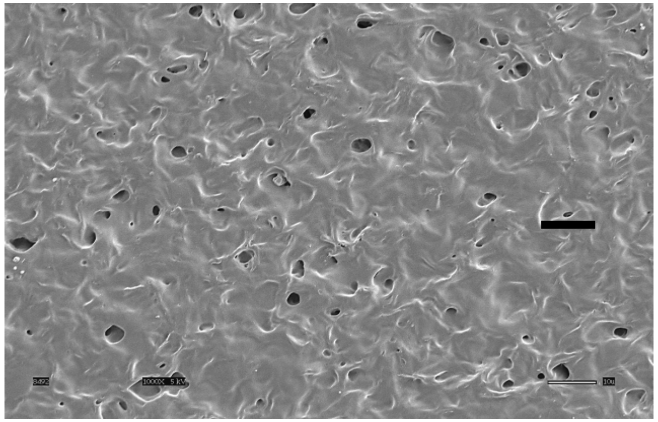


Control (Untreated)

Bar = 10 μm



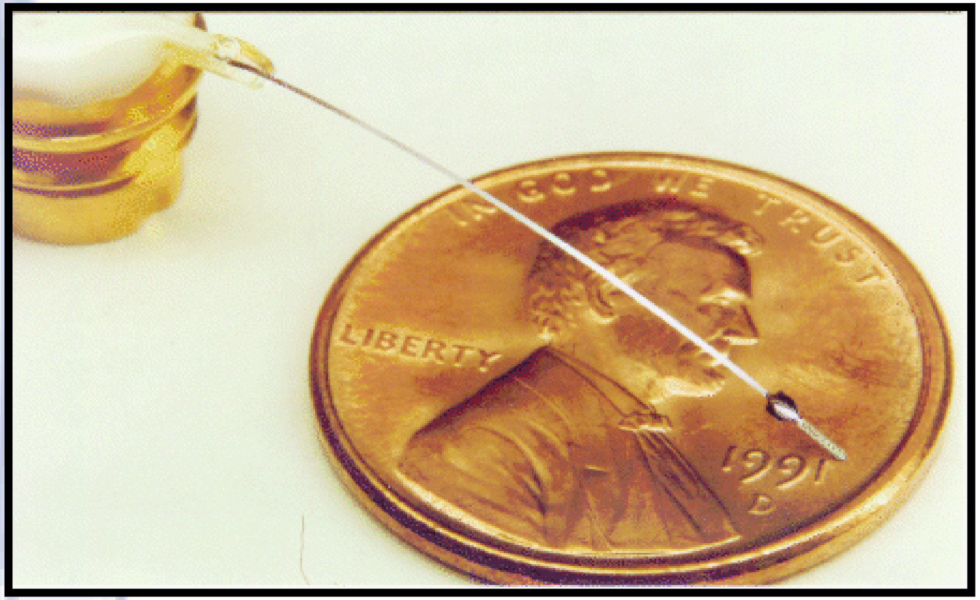
Sub-micron Structured



Nano-structured

PART V
Neural Applications: Nano-structured Silicon and Carbon

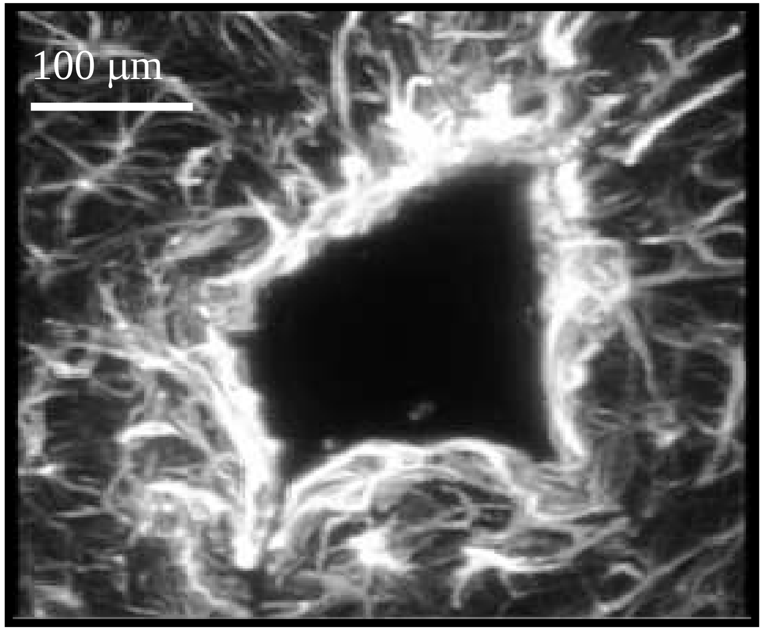
The Problem:
Current Neural Implant Failures



www.engin.umich.edu/facility/cnct/probeback.html

- Chronic probes monitor and apply electrical signals

- Glial scar tissue increases probe impedance

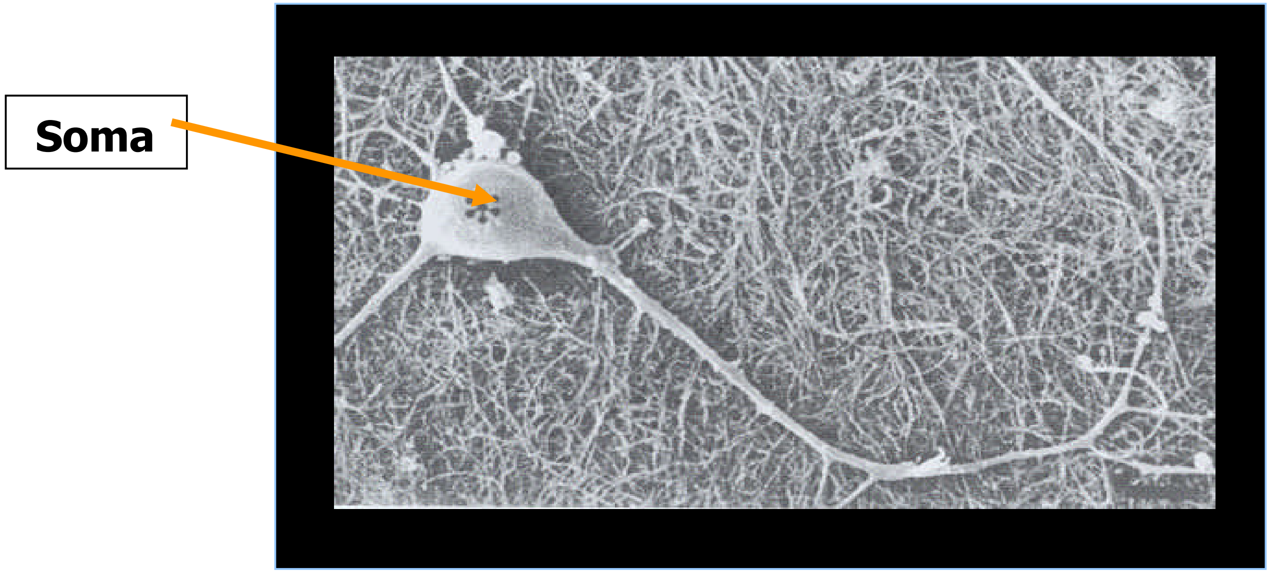


www.cnf.cornell.edu/2001cnfra/20012.pdf

Increased Functions of Neurons on Nanoscale Materials

Neurite outgrowth increased on:

- quartz with nanometer surface roughness,[1]
- nanoscale polystyrene grooved substrates,[2] and
- carbon nanofibers functionalized with 4-hydroxynonenal[3].



[1] Torimitsu et al., ICCE/9 Conference Proceedings 2002:795-6.
[2] Walsh et al., SFB Conference Proceedings 2002:49.
[3] Mattson et al., J Mol Neuroscience 2000;14:175-82.

Design of Carbon Nanofibers for Neural Implants

- Decreased functions of astrocytes on smaller dimension carbon nanofibers.
- Decreased functions of astrocytes on polymer composites containing increased amounts of carbon nanofibers.

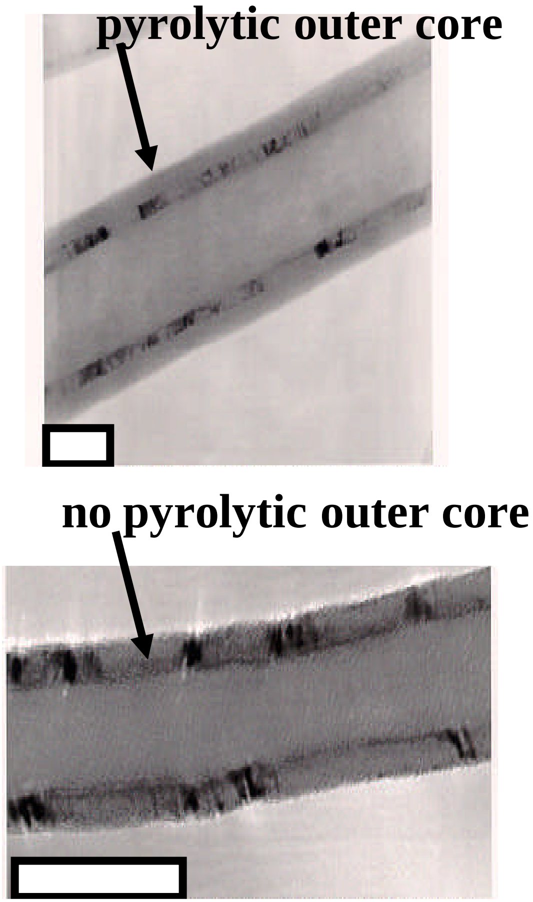
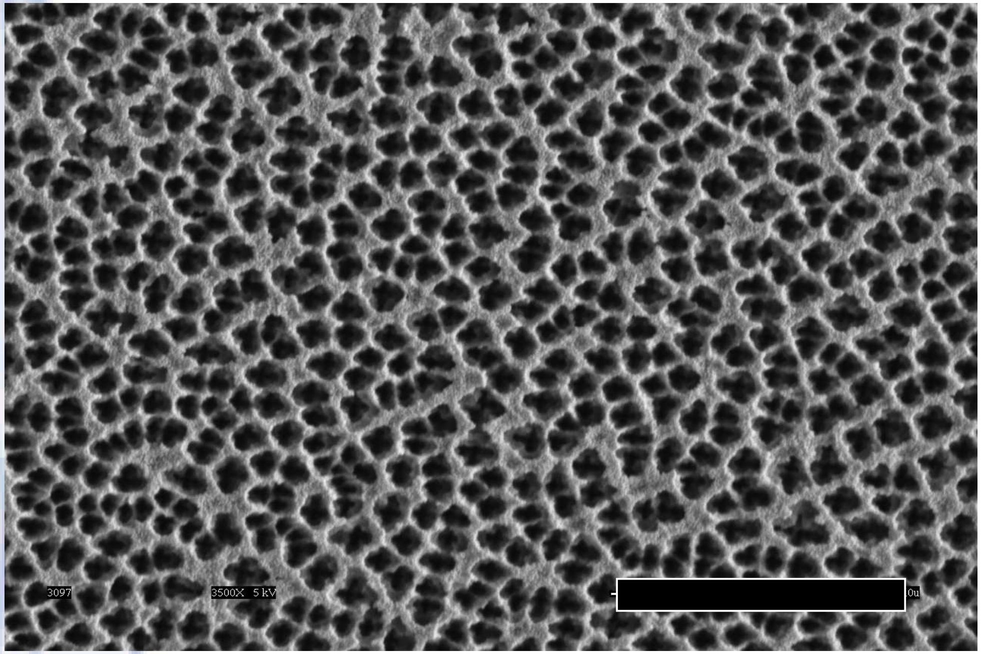


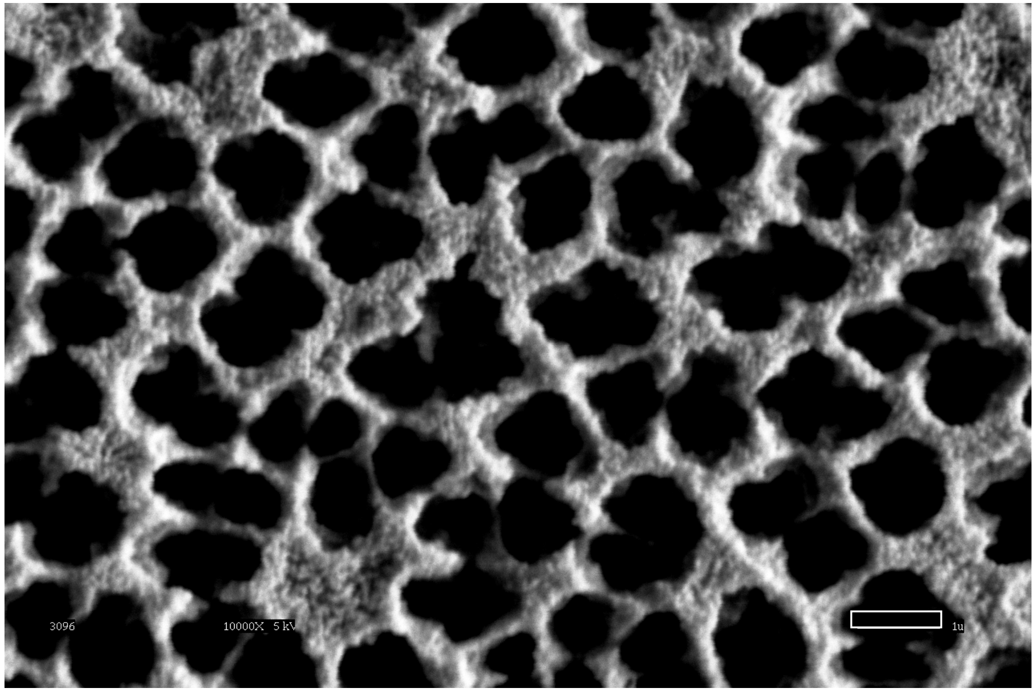
Figure: TEM of Individual Carbon Nano-dimensional Fibers
Bar = 100 nm.

J. L. Mckenzie, M. C. Waid, R. Shi, T. J. Webster, "Cytocompatibility of astrocytes on carbon nanofibers," *Biomaterials* , available on-line, 2004.

Increased Functions of Neurons and Decreased Functions of Glial Cells on High Porous Silicon

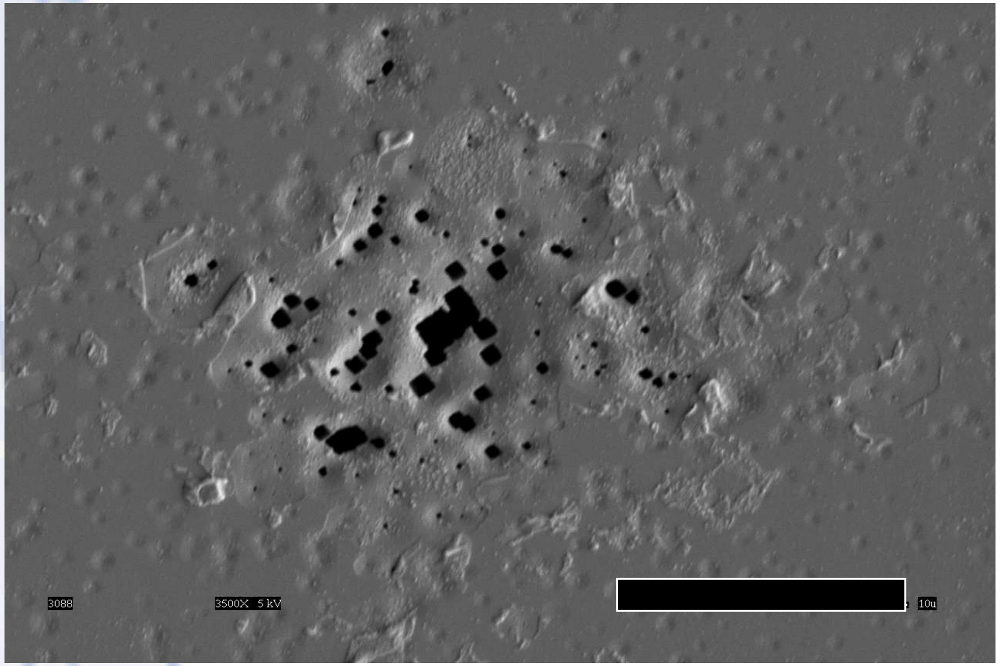


Scale bar = 10 µm

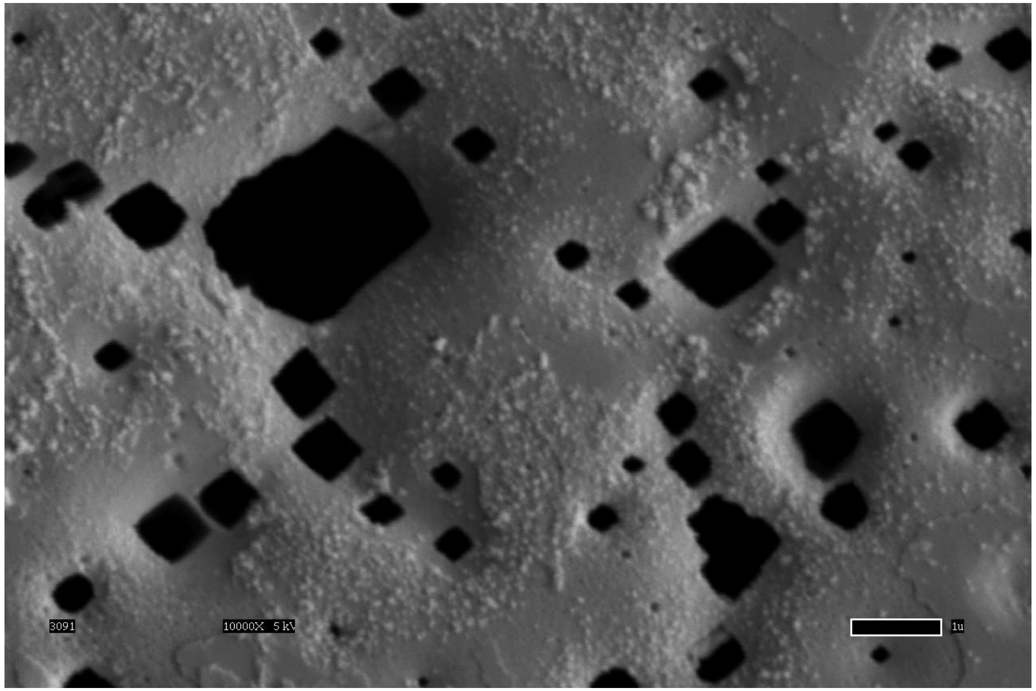


Scale bar = 1 µm

Increased Functions of Neurons and Decreased Functions of Glial Cells on Low Porous Silicon

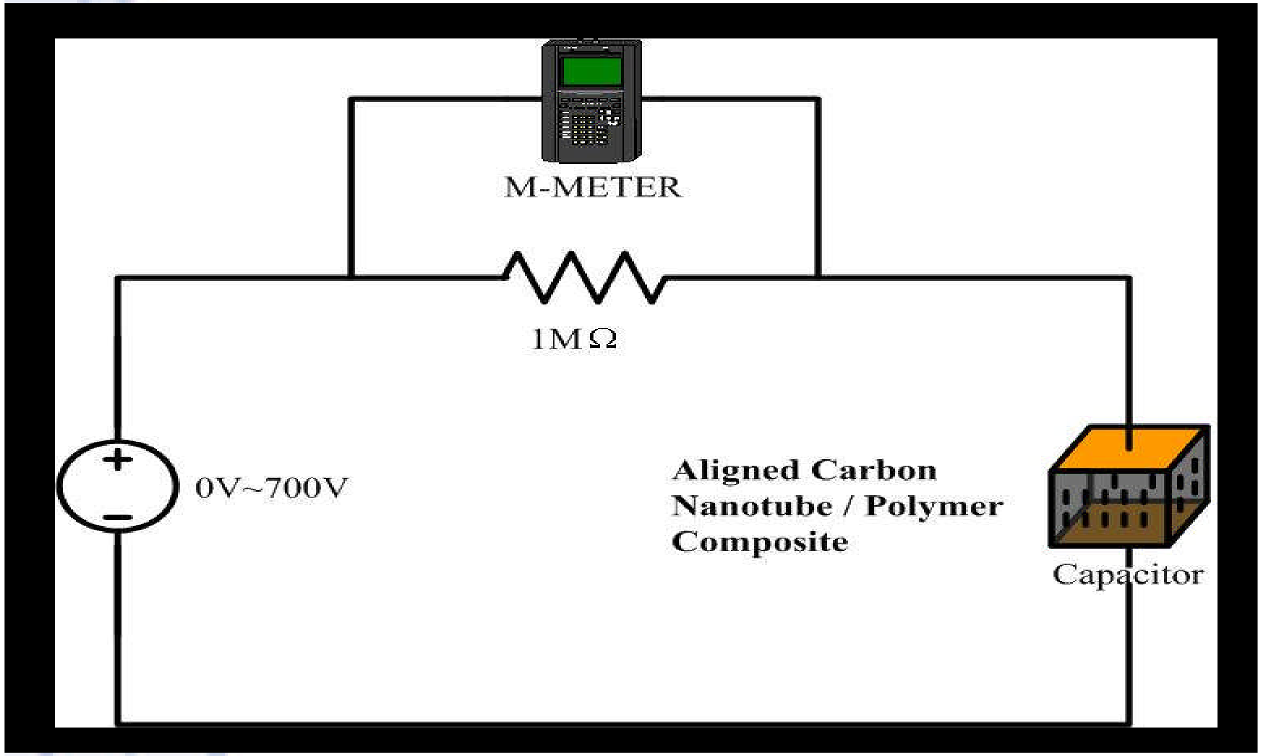


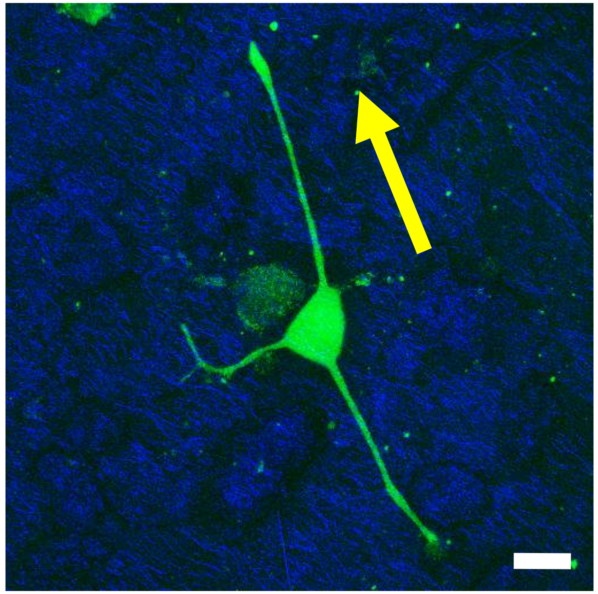
Scale bar = 10 μm

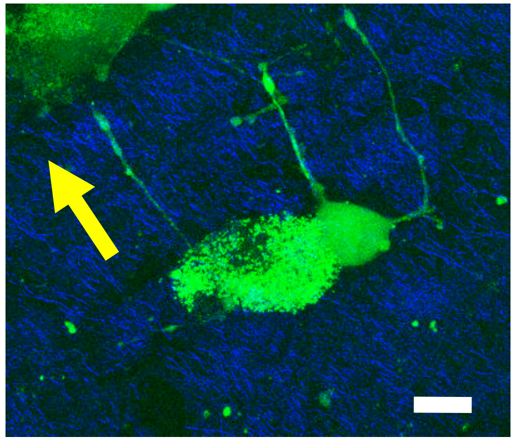


Scale bar = 1 μm

Aligned Neurite Extensions on Aligned Carbon Nanofibers in Polymer Matrices



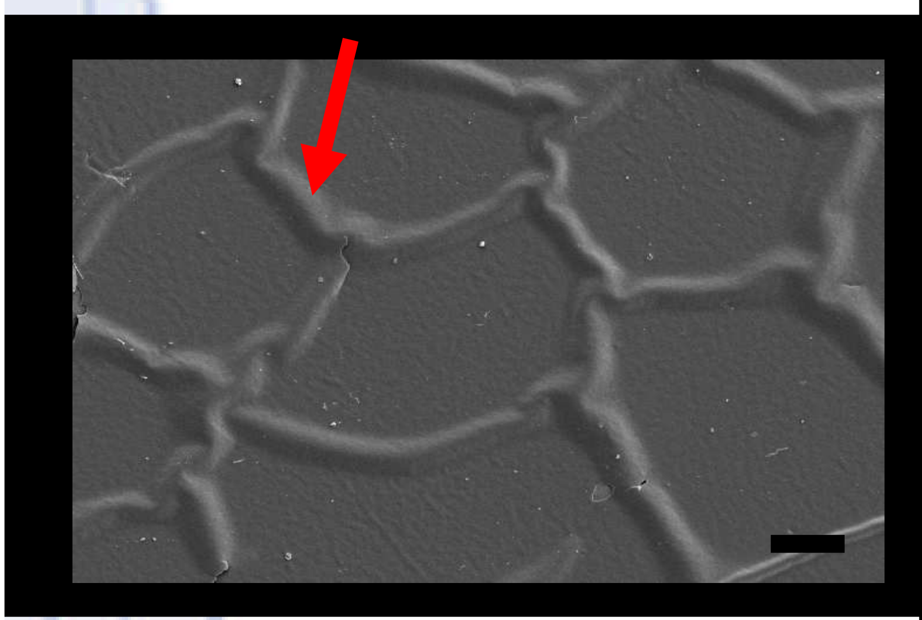




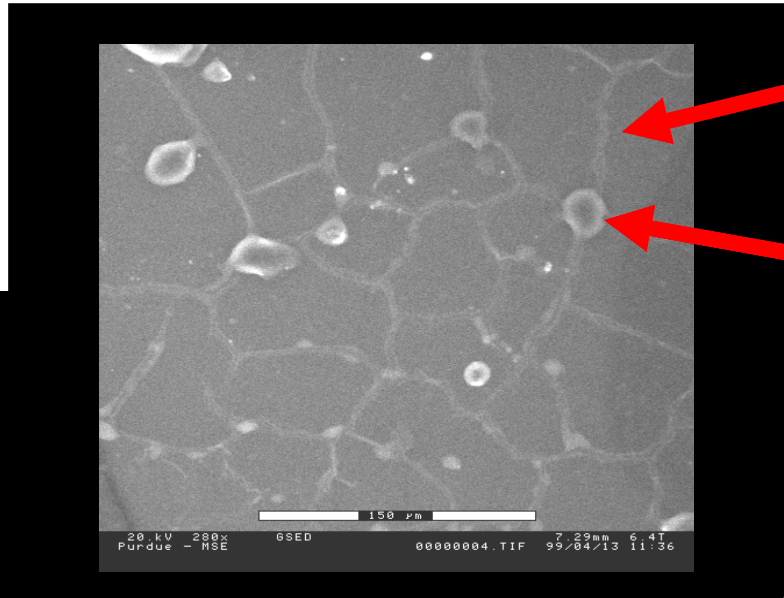
Bar = 20 microns.

Directed Axonal Outgrowth of Neurons on Carbon Nanofiber:Silicon Composites

Carbon wormy buckles deposited on silicon



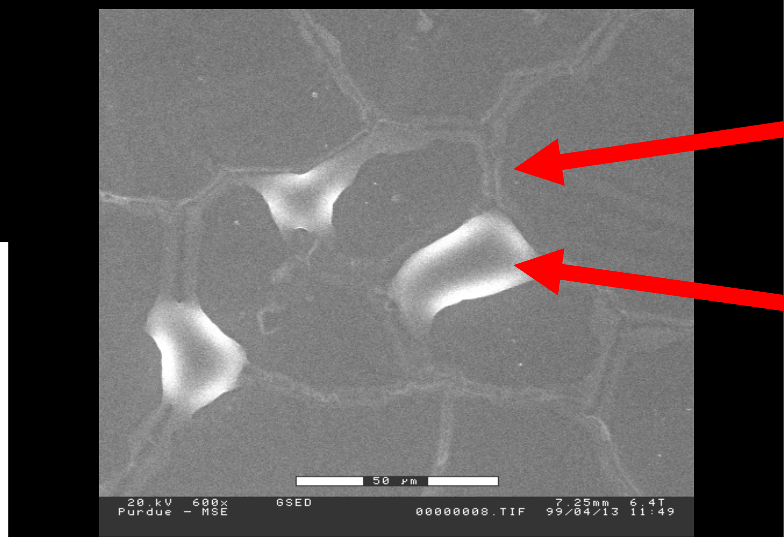
Scale bar = 10 µm



Neuron axon alignment

Neuron

Scale bar = 150 and 50 microns on top and bottom, respectively.



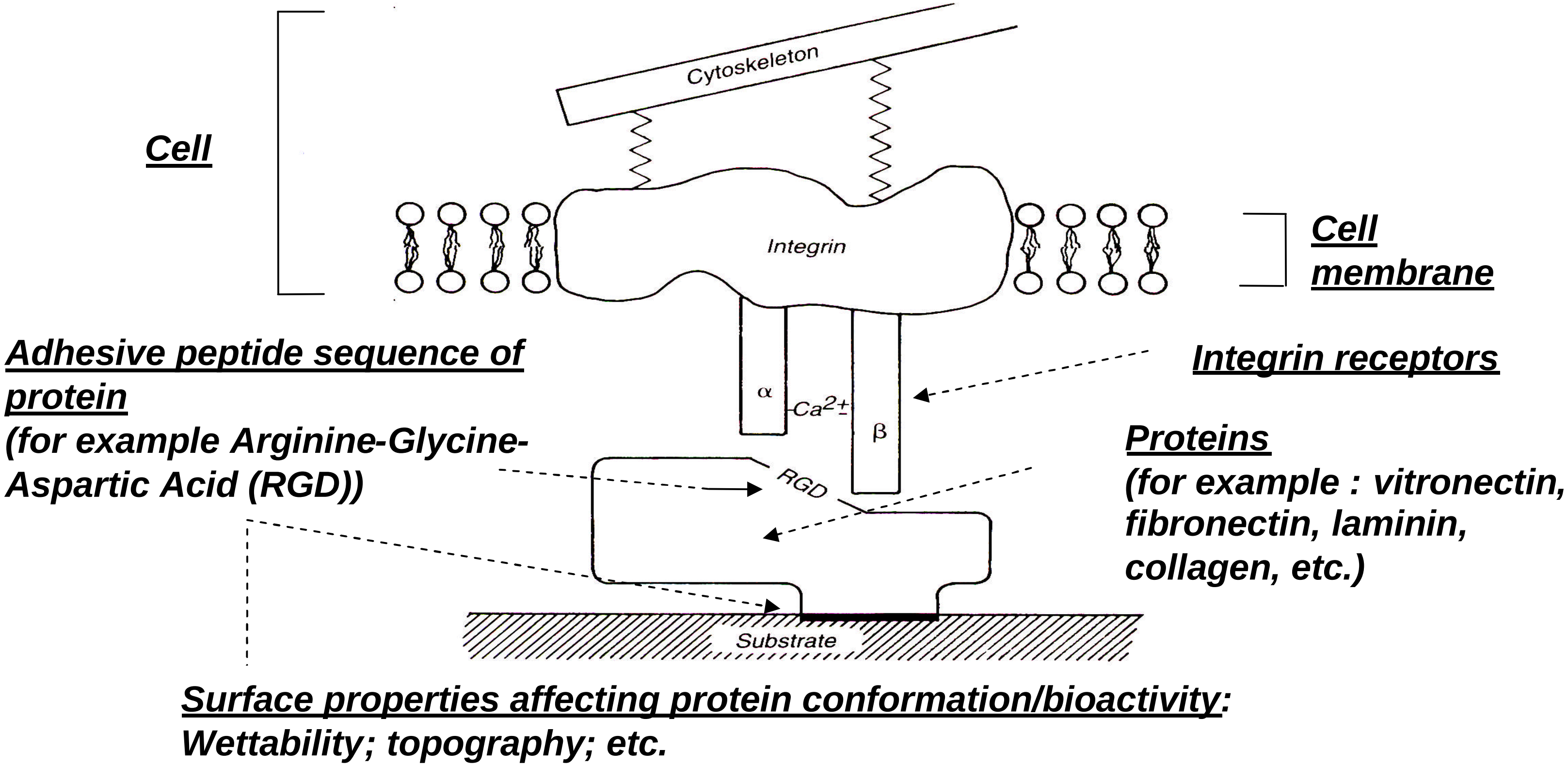
Neuron axon alignment

Neuron

Discussion

- There is now a large amount of evidence that cells respond differently to nano-structured compared to conventional surfaces.
- In all applications, the over-riding design parameter is to create a nano-structured surface whether by changing constituent particle size or altering just the surface features.
- Nano-structured materials possess higher percentages of atoms at the surface, increased portions of surface defects, and greater numbers of material boundaries at the surface that may be influencing protein interactions important for cell function.

Nanophase Materials Enhance Availability of Cell-adhesive Domains of Proteins to Promote Subsequent Cell Function



Adapted and redrawn from Schakenraad, J.M . pp. 140-141, in *Biomaterial Science (B. Ratner et al., eds.),*Academic Press, Inc., San Diego, CA, 1996.

T. J. Webster, C. Ergun, R. H. Doremus, R.W. Siegel, and R. Bizios, *Journal of Biomedical Materials Research* 51:475-483 (2000); T.J. Webster, L.S. Schadler, R.W. Siegel, R. Bizios, *Tissue Engineering* 7:291-301 (2001).

Potential Problems

- However, there are many potential problems with the use of nanophase materials in the body that still need to be determined.

- Some of these include:
    - Cost of fabrication,
    - Impurities in fabrication techniques,
    - Influence of wear debris,
    - Corrosion, and
    - Overall *in vivo* response.

- Despite these potential problems, due to the large body of evidence of increased tissue regeneration on nano-structured surfaces, these potential problems should not be overlooked.

Conclusions

- **Compared to conventional materials, nano-spherical ceramics, nanophase ceramic/PLGA composites, nano-fibered ceramics, carbon nanofibers, carbon nanofiber/PU composites, and sub-micron structured metals enhanced functions of cells pertinent for bone, cartilage, vascular, bladder, and neural applications.**

- **Due to their ability to biomimic fundamental constituent dimensions of natural tissue, nano-structured materials have the potential to become the next-generation of hard implant materials with increased efficacy.**

THANK YOU !!