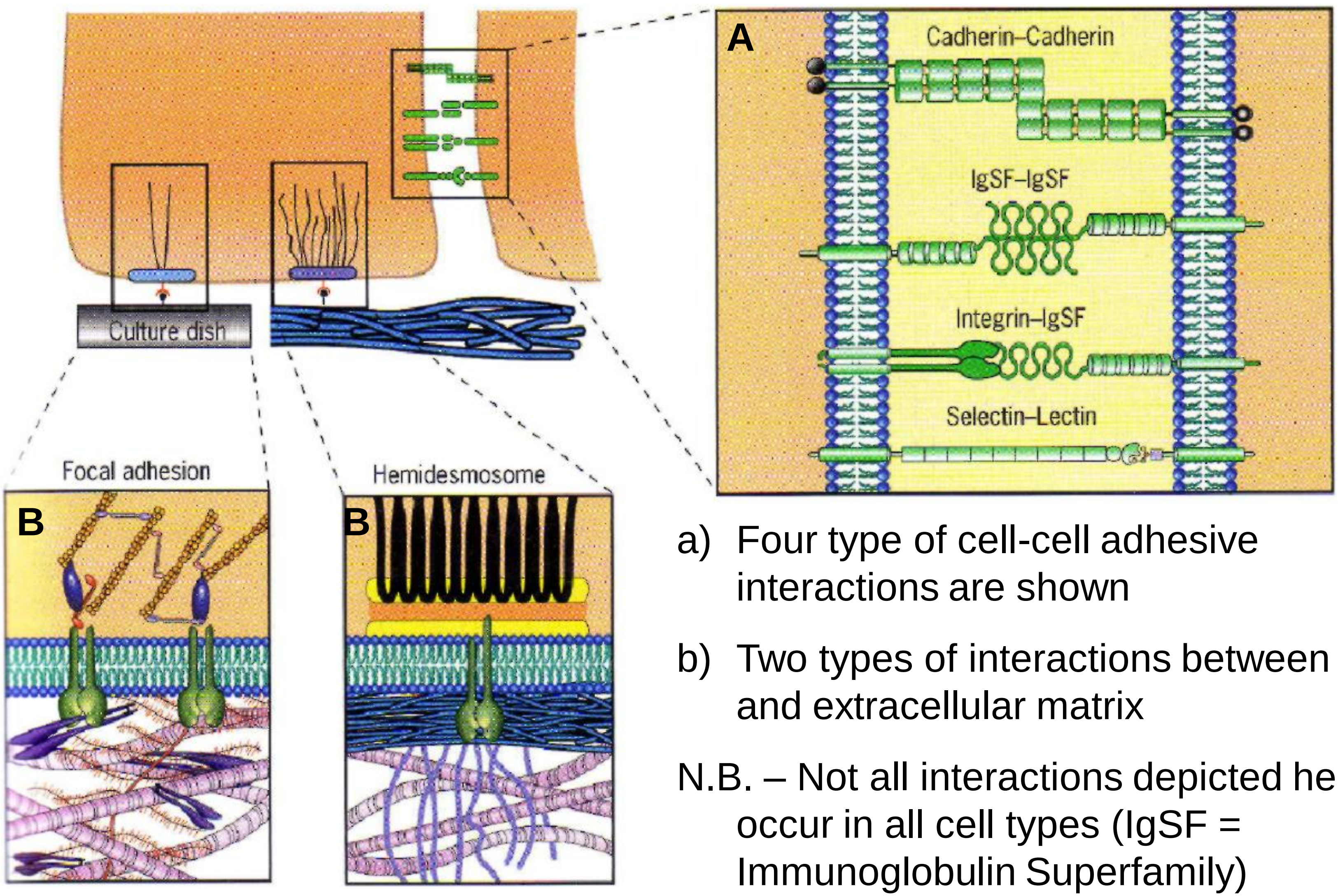
Cell Surface Interactions

Introduction to Cell/Surface Interactions

- The biomedical response to the introduction of an implant is controlled by the interaction between the cell and the implant's surface
- These interactions occur at multiple scales:
  - Meso
  - Micron
  - Sub-micron
  - Atomic

Biochemical Structure of the Interface



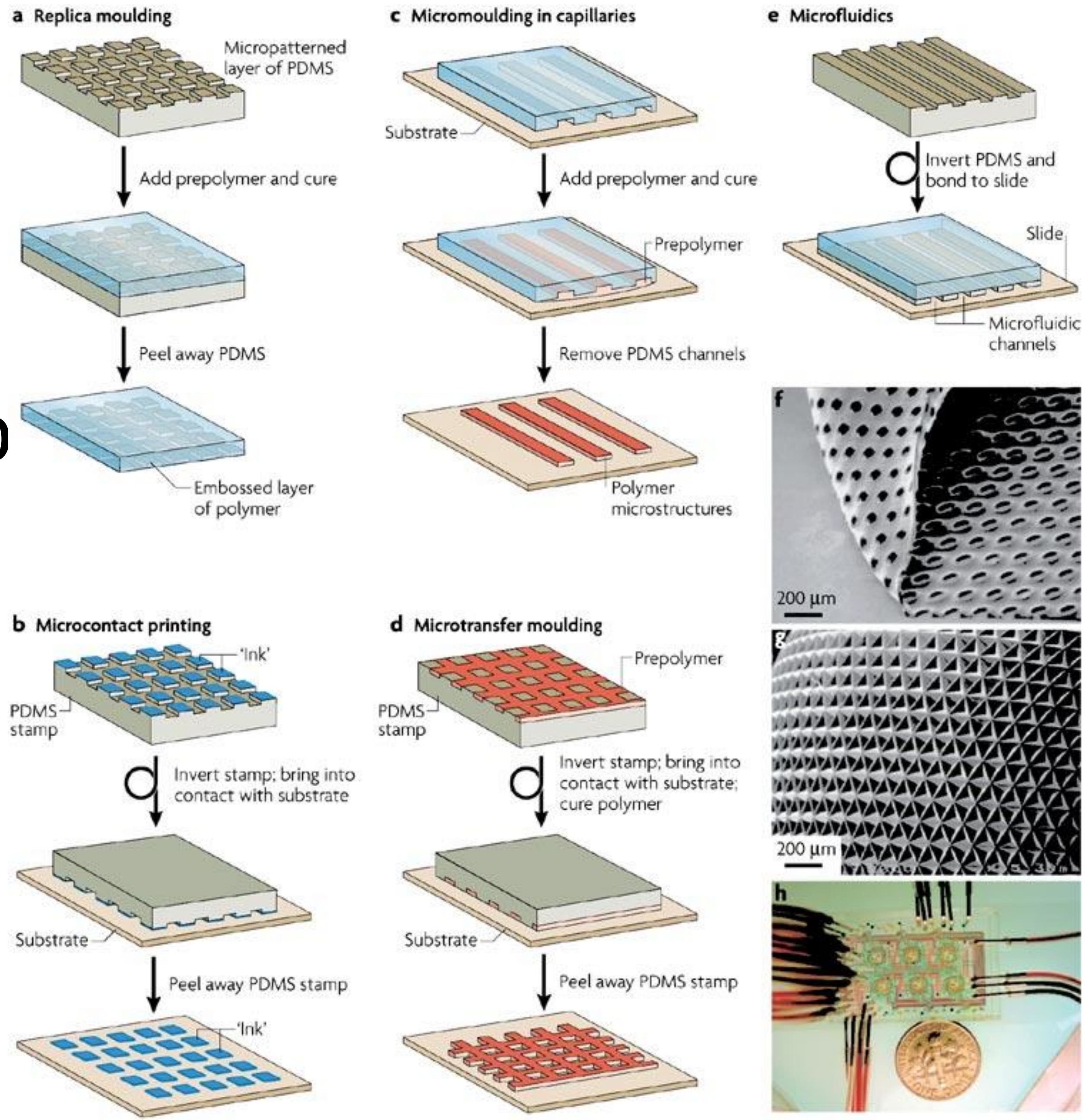
a) Four type of cell-cell adhesive interactions are shown

b) Two types of interactions between cells and extracellular matrix

N.B. – Not all interactions depicted here do occur in all cell types (IgSF = Immunoglobulin Superfamily)

Karp 7.28, 2004

Introduction to Patterned Biomedical Surfaces



Weibel *et al.* *Nature Reviews Microbiology* **5**, 209–218 (March 2007) | doi:10.1038/nrmicro1616

Application of Ti-6Al-4V in the Human Body

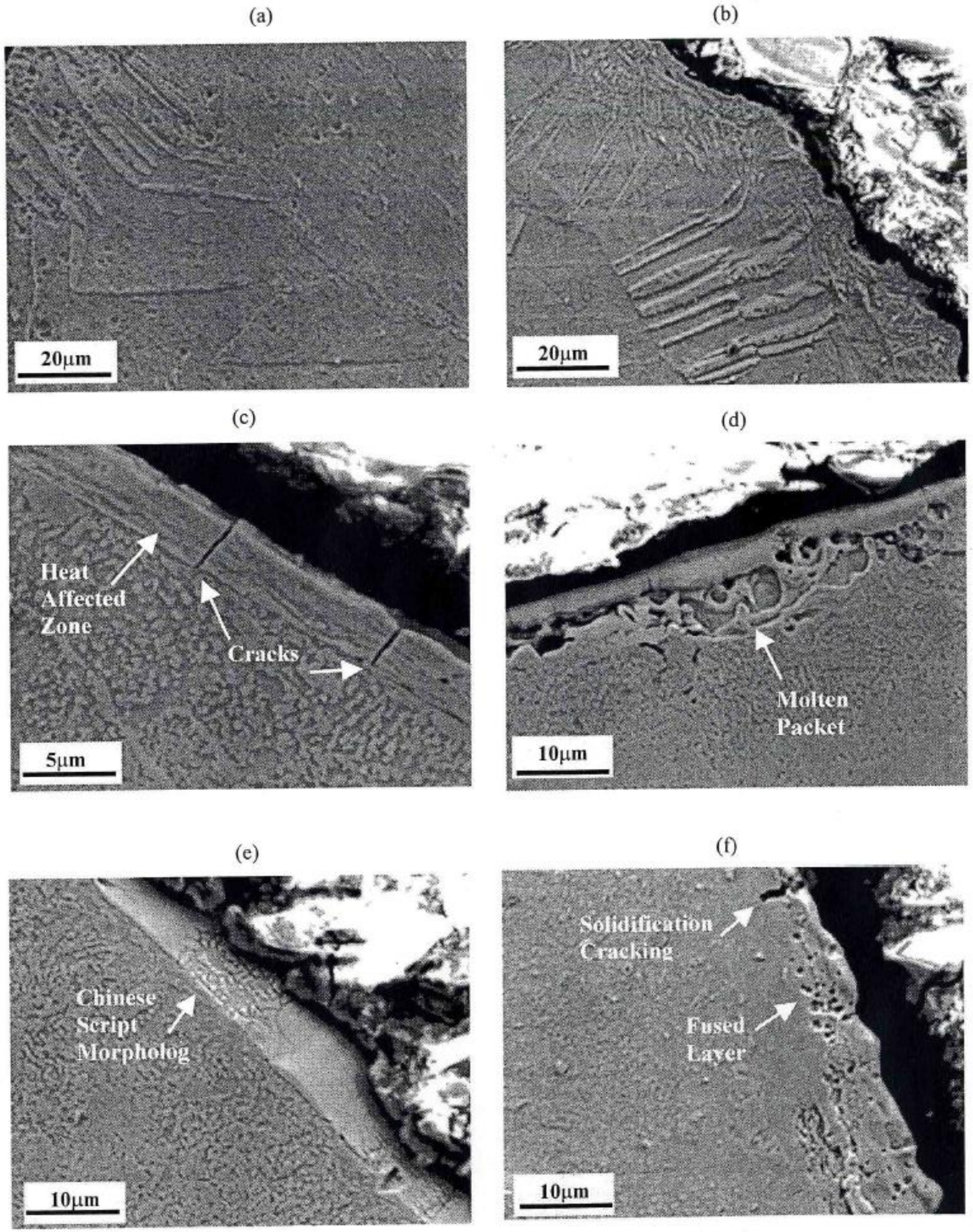
- Hip, knee, and dental implants – prosthetic devices
  - Several million people need implants every year
  - Problem is that the implants last only ~10-20 years
  - Implants often require major invasive surgeries
    → Mostly prescribed for older patients

Attachment of Titanium Implants to Cells

- Titanium is one of the few metals that is not toxic to the human body
- Hence, widespread and increasing use of titanium and titanium alloys in prosthetic devices, e.g. Ti-6Al-4V, Ti-6Al-7Nb
  - tooth implants
  - hip implants (both dogs and humans!)

- Attachment of metal to cells is strongly dependent on hierarchy of size scales
  - molecular attachment to protein molecules
  - size of cells compared to grain size
  - size of cells compared to laser groove size

SEM of Ti-6Al-4V Specimens



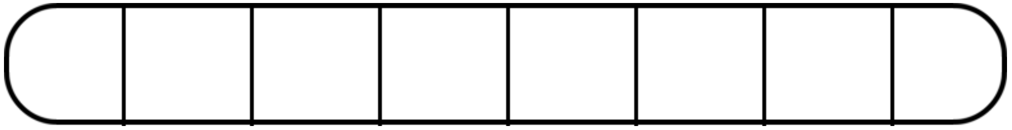
SEM micrographs of Ti-6Al-4V specimens;

(a) bulk material of polished specimen;
(b) outer edge of grit blasted specimen;
(c) heat affected zone, fused layer and solidification cracking in 8µ circumferentially grooved specimen;
(d) example of moiten pocket of 8µ circumferentially grooved specimen;
(e) heat affected zone, fused layer, and solidification cracking in 12µ circumferentially grooved specimen;
(f) heat affected zone, fused layer, and solidification cracking in 12µ longitudinally grooved specimen

Schematic Illustration of Textured Ti-6Al-4 Surfaces

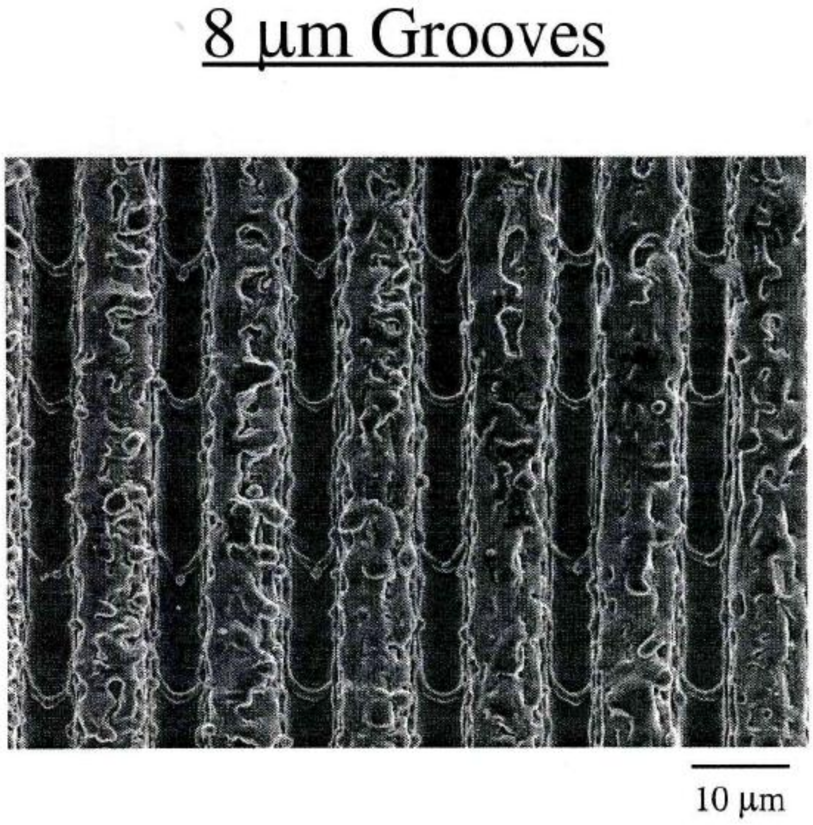
- Control Surfaces were produced by grit blasting and polishing
- Experimental surfaces for tooth and hip implants were produced by grit blasting, polishing and laser processing
- Initial characterization of surfaces were done by SEM

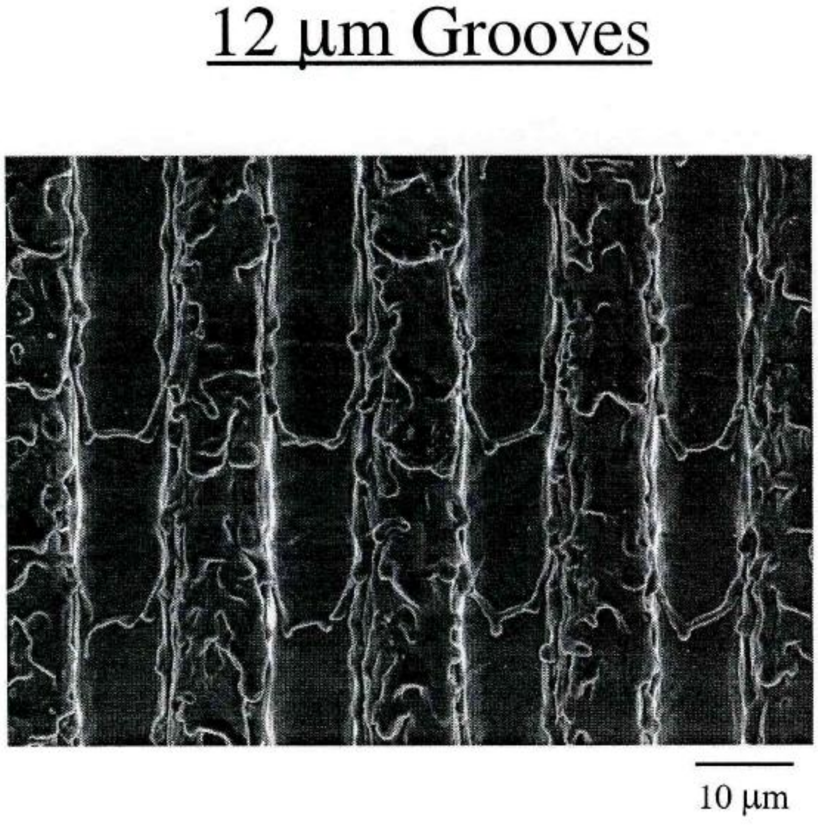
Control Implant Configuration



Experimental Implant Configuration

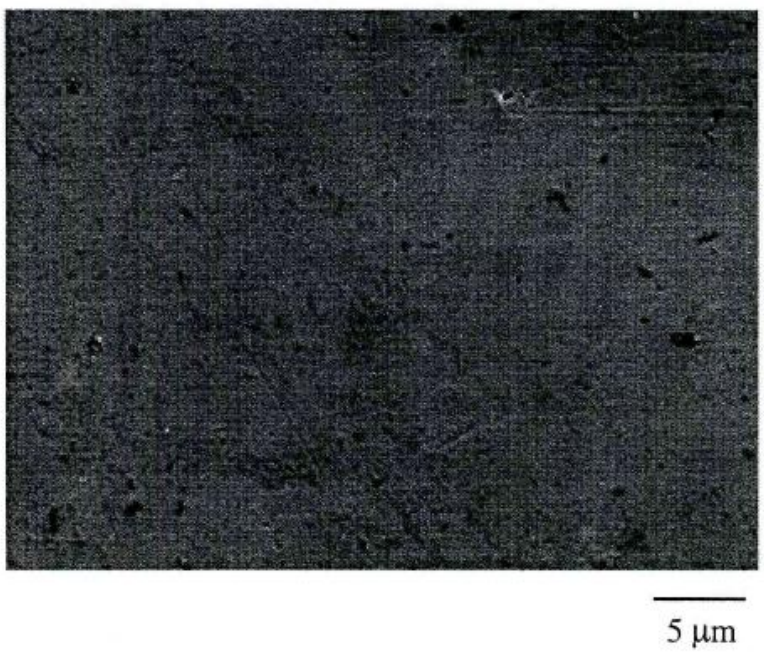
Scanning Electron Micrographs of Dental Ti-6Al-4V Implant



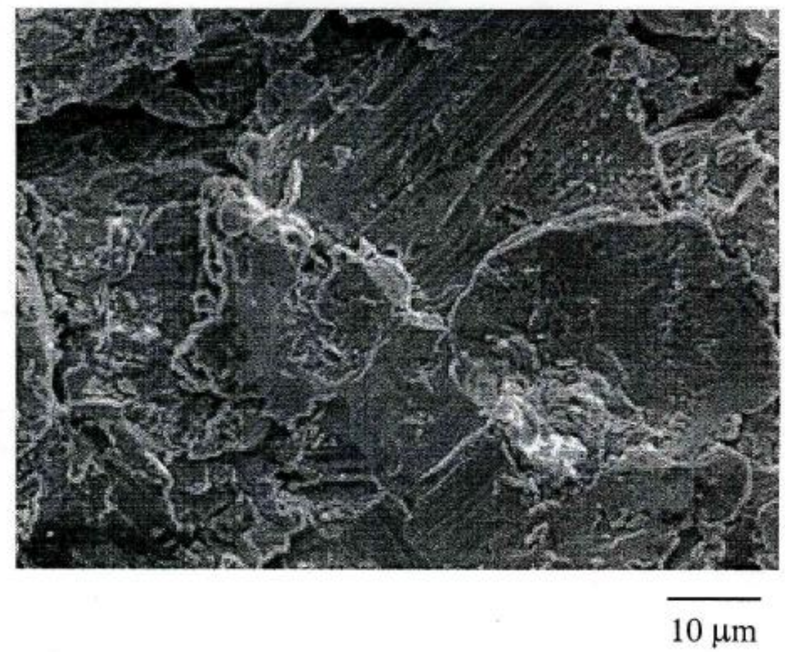


SEM of Polished Surfaces vs Conventional Alumina Blasted Surface

Polished Surface



Alumina Blasted Surface



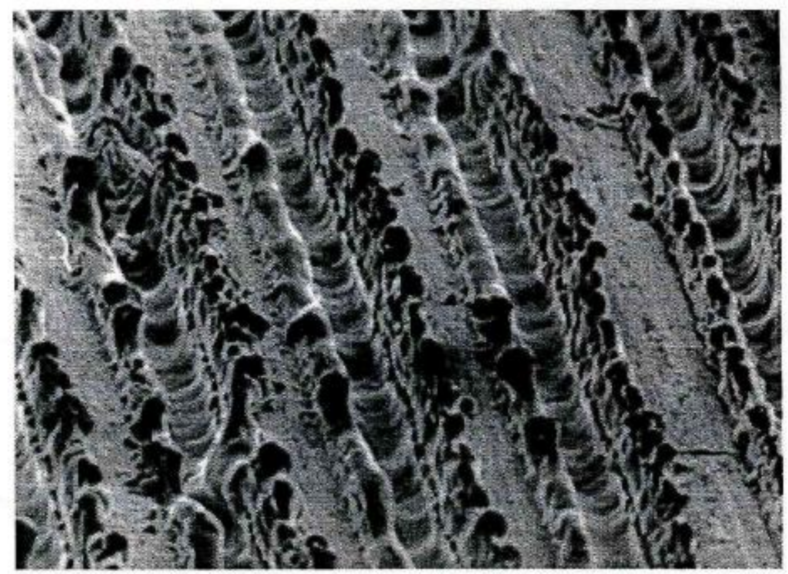
SEM of Textured “dogbone” Ti-6Al-4V

---Dogbone picture here---

8 μm Grooves

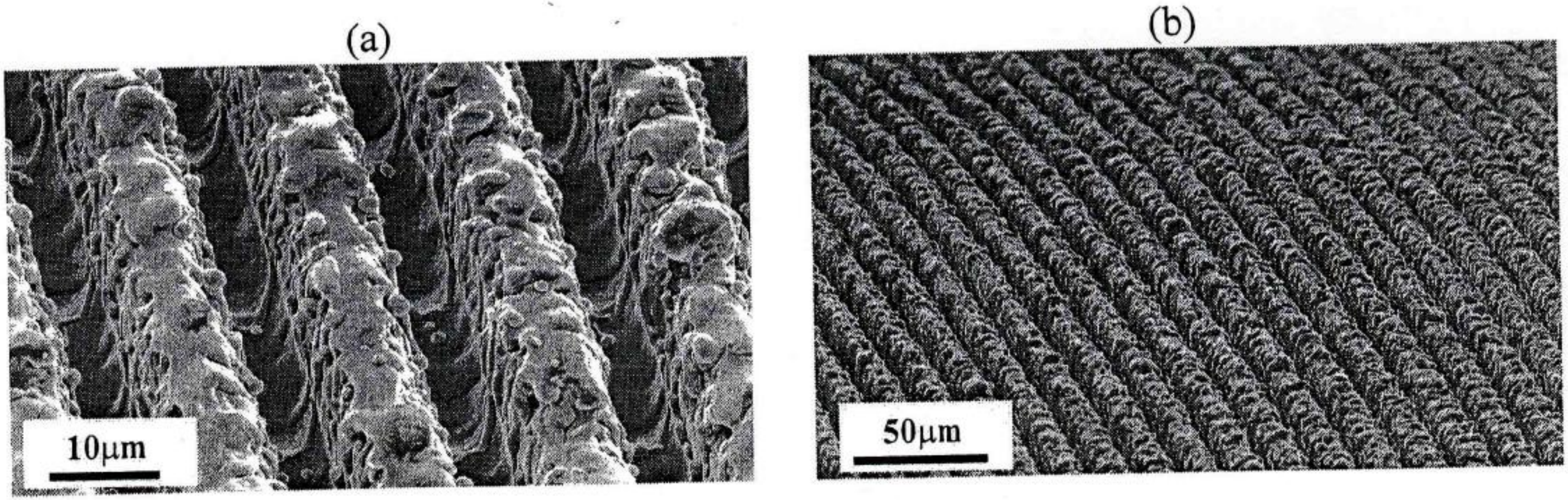
10 μm

12 μm Grooves



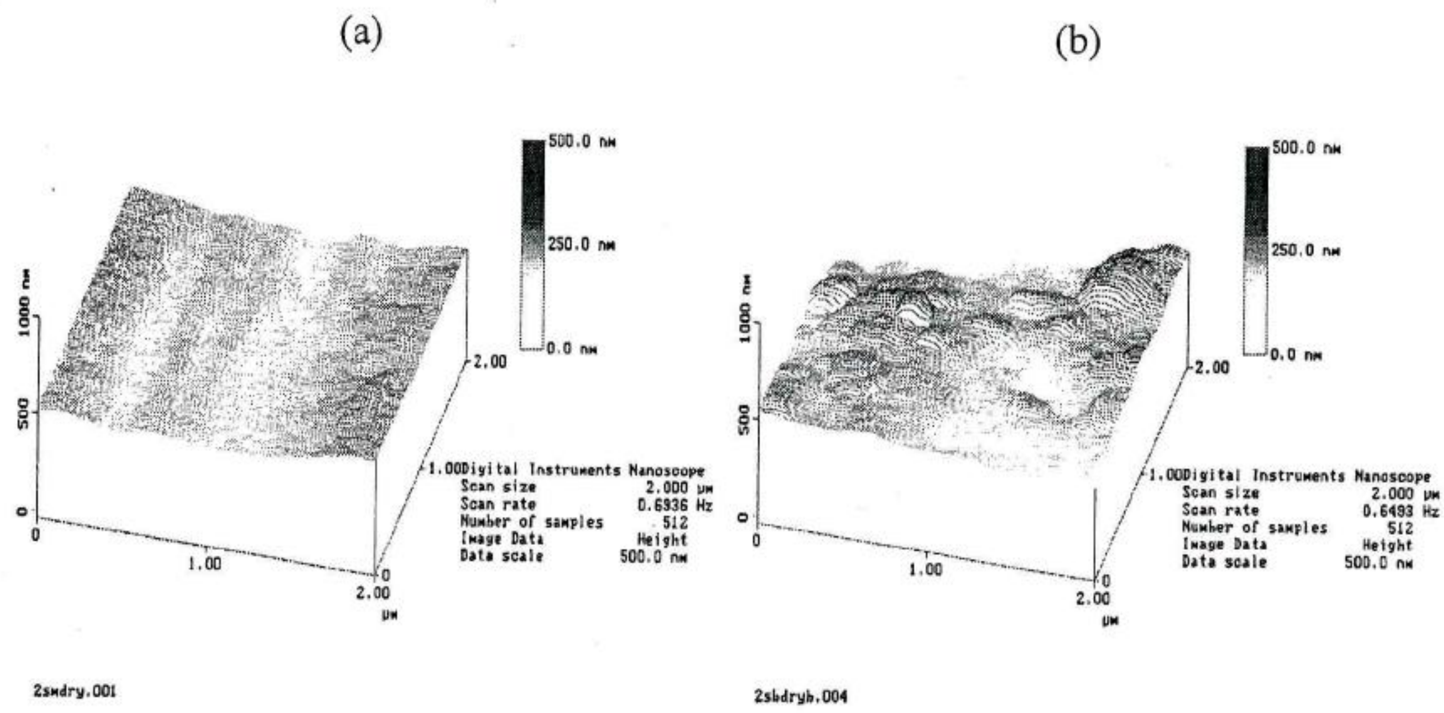
10 μm

SEM of Textured Ti-6Al-4V Surfaces



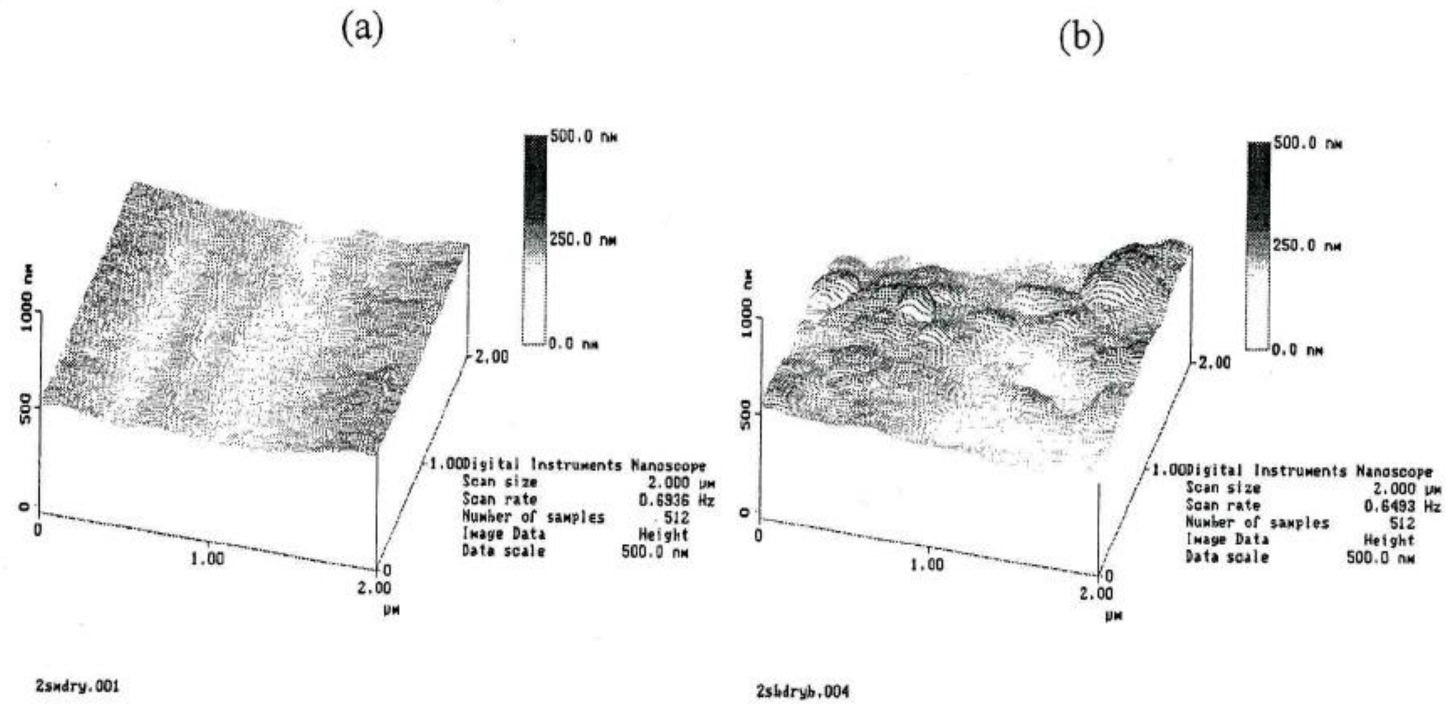
SEM photos of circumferential laser ablated grooves: (a) Longitudinal grooves and (b) Circumferential grooves

Atomic Force Microscopy Images of Textured Ti-6Al-4V Surfaces



Tapping mode AFM images: (a) Polished surface and (b) Alumina blasted surface

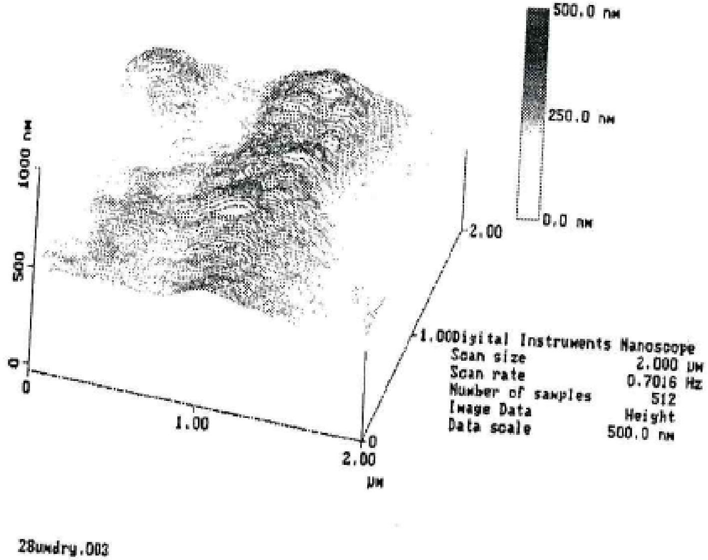
Atomic Force Microscopy Images of Textured Ti-6Al-4V Surfaces



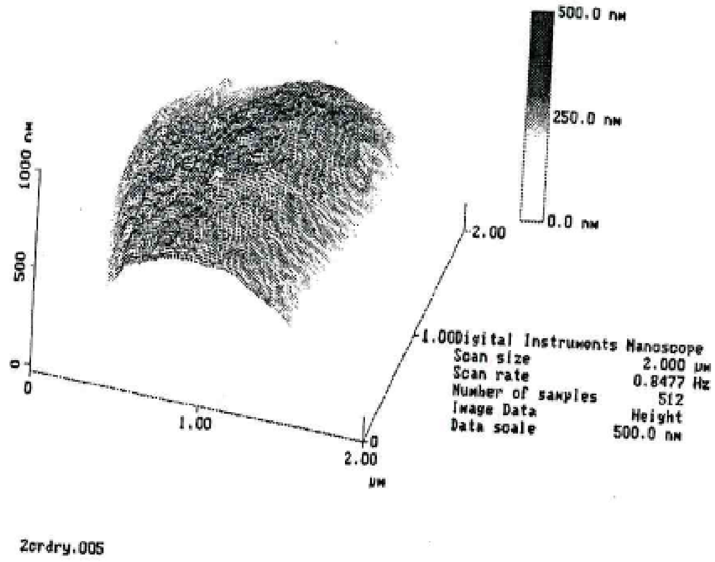
Tapping mode AFM images: (a) Polished surface and (b) Alumina blasted surface

Atomic Force Microscopy Images of Textured Ti-6Al-4V Surfaces

(a)



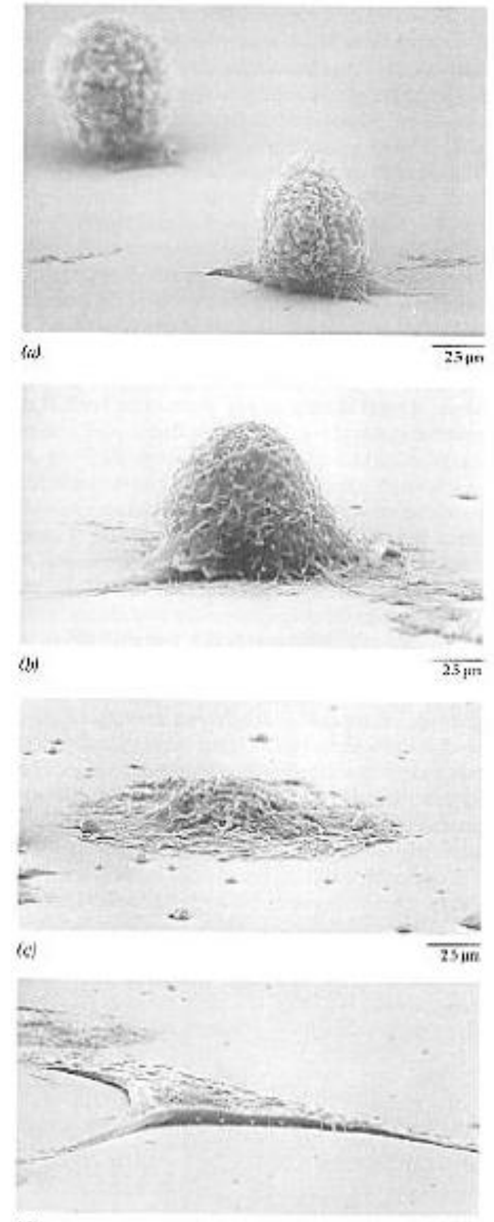
(b)



Tapping mode AFM images of laser textured surfaces: (a) Peak of 8 micron grooves and (b) peak of 12 micron grooves

Introduction to Cell/Surface Interactions

- Cells in suspensions exhibit spherical morphology *(a)*
- Upon contact to a receptive surface, cells start to spread *(b)*
- Spreading continues until cells is properly "anchored" *(c)*
- Once attachment is completed, cells can migrate to areas of higher cell surface affinity *(d)*
  - Done through fillopodiums and lamellipodiums (extension of the cytoplasm)

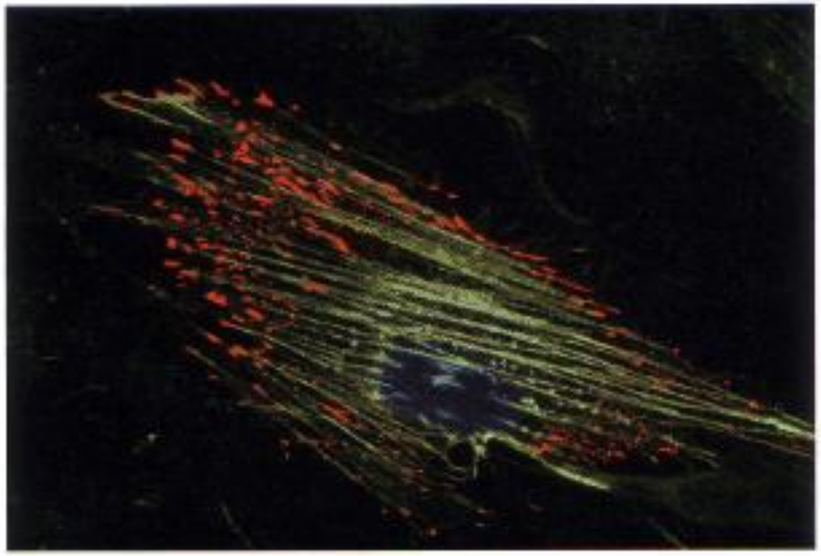


Karp 7.16

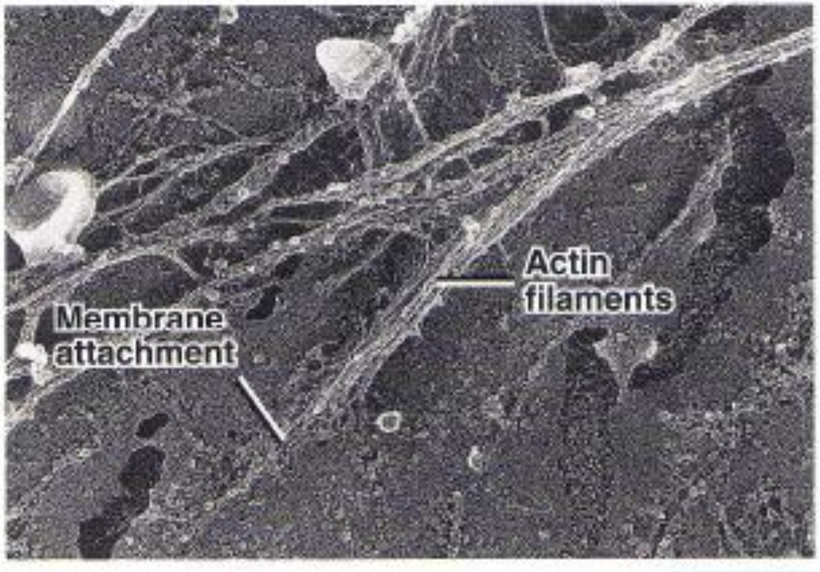
Introduction to Cell/Surface Interactions

- Cell / surface interaction is achieved through focal adhesion points:
  - An agglomeration of multiple proteins from the extracelular matrix (ECM) and trans-membrane proteins

Major Focal Adhesion Point Proteins	
ECM	Trans-Membrane
Collagen	Actin/Actin filament
Fibronectin	Vinculin
Laminin	Integrin



(a)



(b) 2.5 µm

Cell and Molecular Biology, G. Karp 2004

Introduction to Cell/Surface Interactions

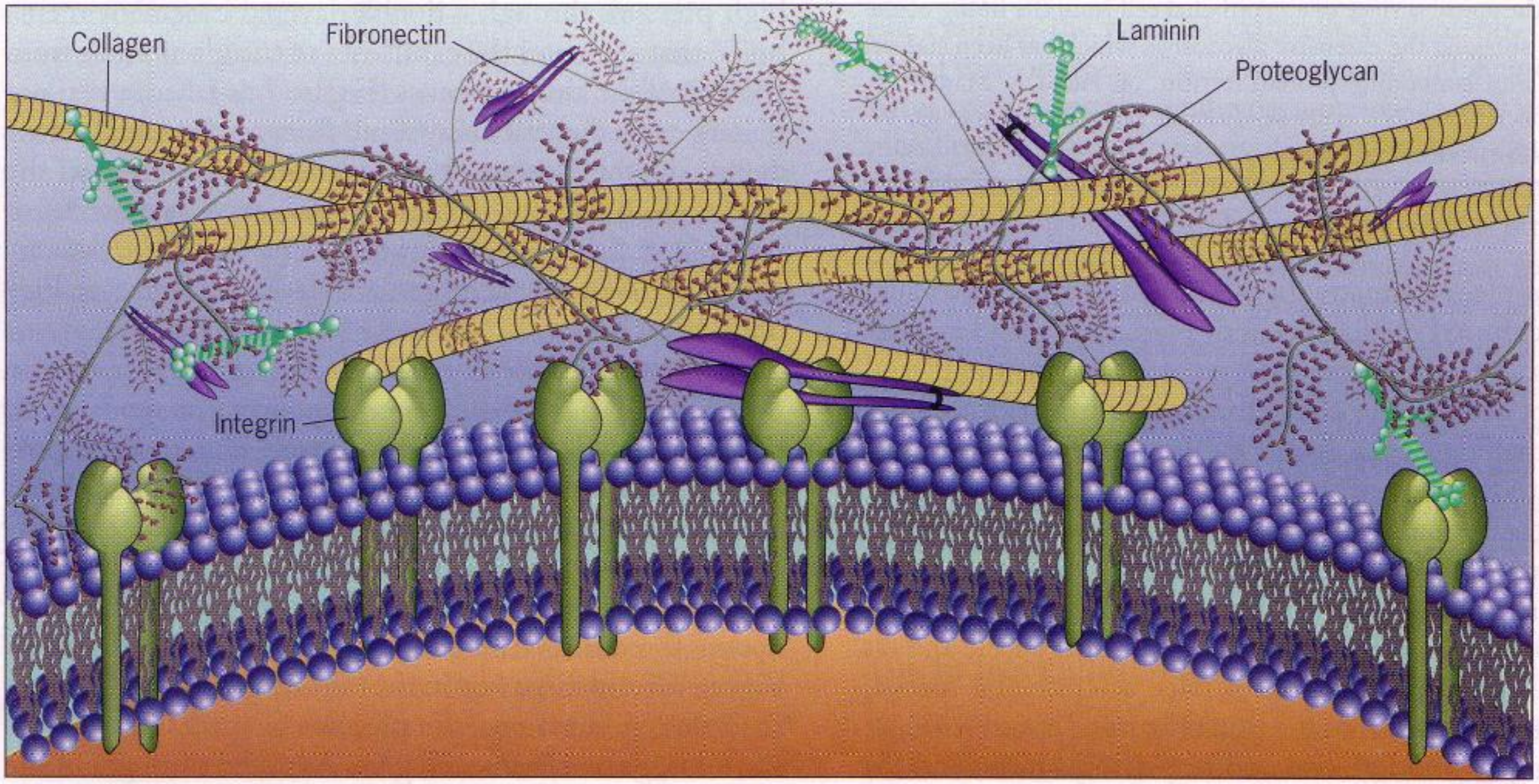
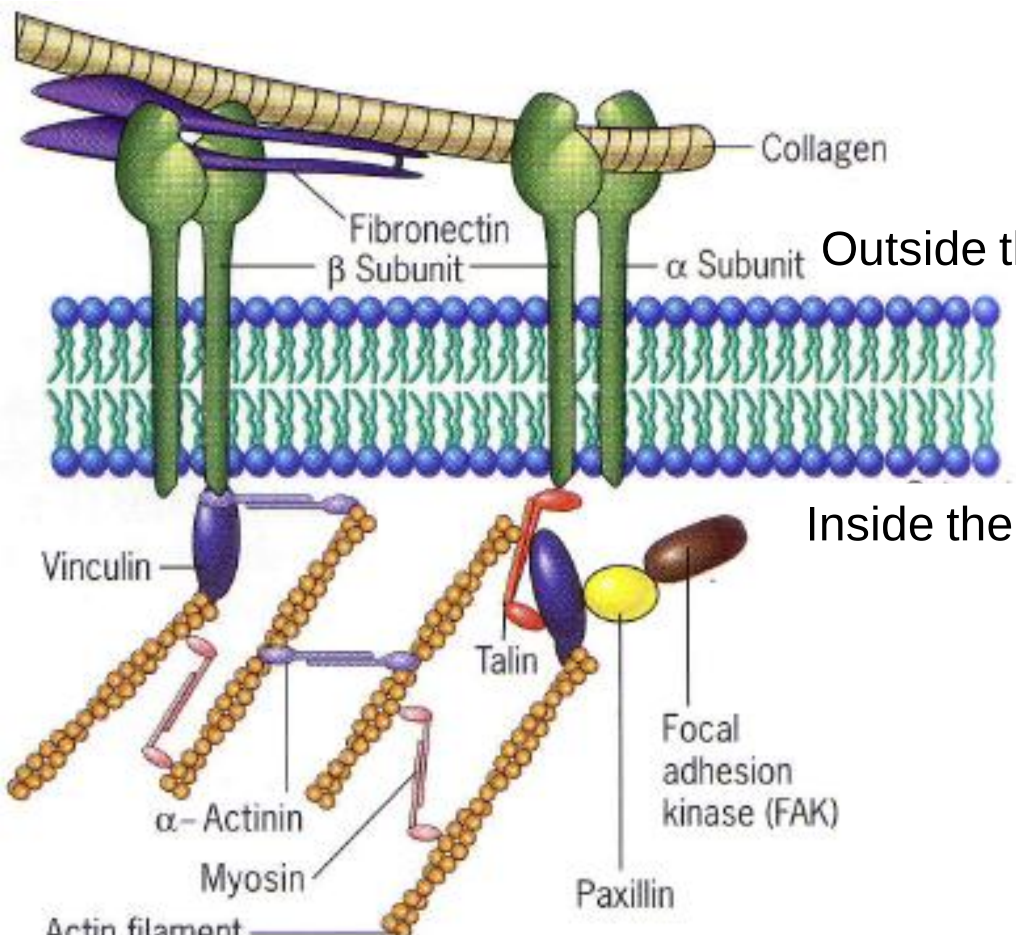


FIGURE 7.5 An overview of the macromolecular organization of the extracellular matrix. The proteins and polysaccharides shown in this illustration will be discussed in the following sections. The proteins depicted (fibronectin, collagen, and laminin) contain binding sites for one another, as well as binding sites for receptors (integrins) that are located at the cell surface. The proteoglycans are huge protein–polysaccharide complexes that occupy much of the volume of the extracellular space.

Cell and Molecular Biology, G. Karp 2004

Introduction to Cell/Surface Interactions

Protein Interaction at a Focal Adhesion Point



Cell and Molecular Biology, G. Karp 2004

Introduction to Cell/Surface Interactions

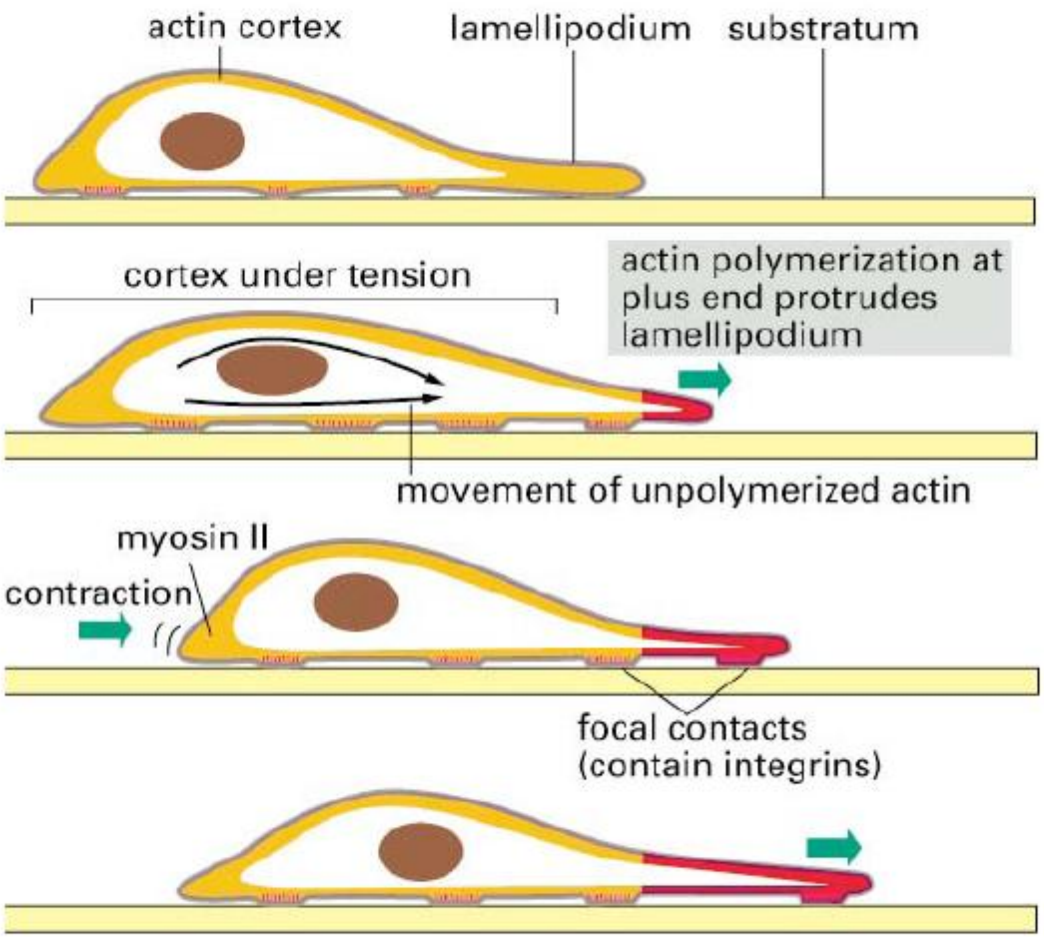
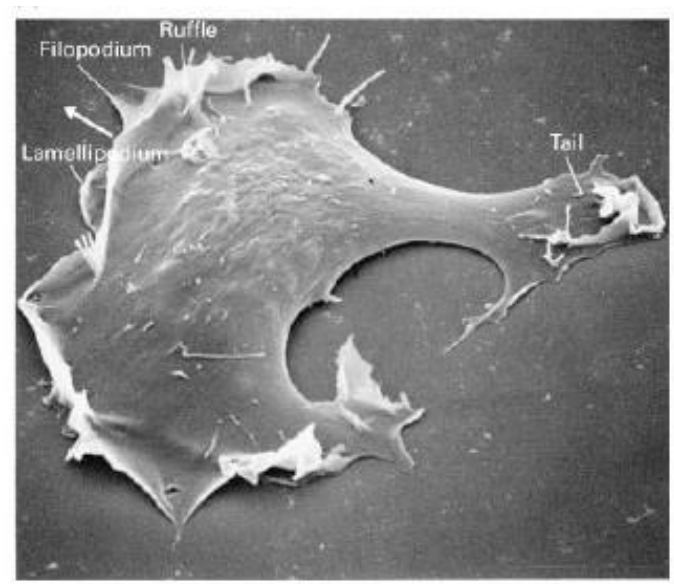
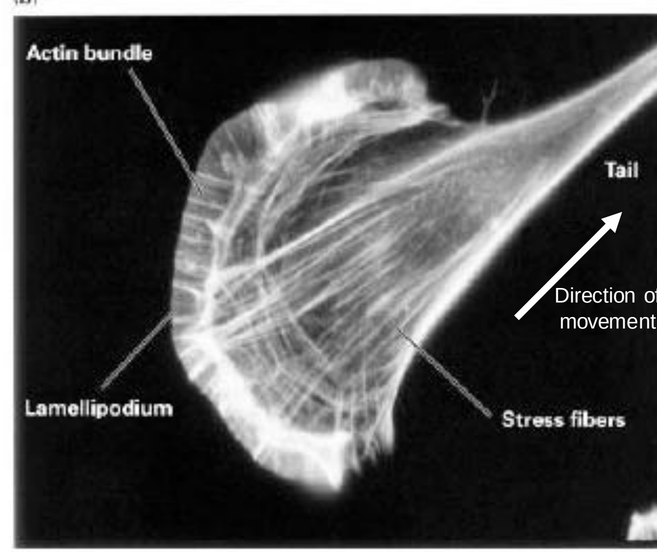


Figure 16–85. Molecular Biology of the Cell, 4th Edition.

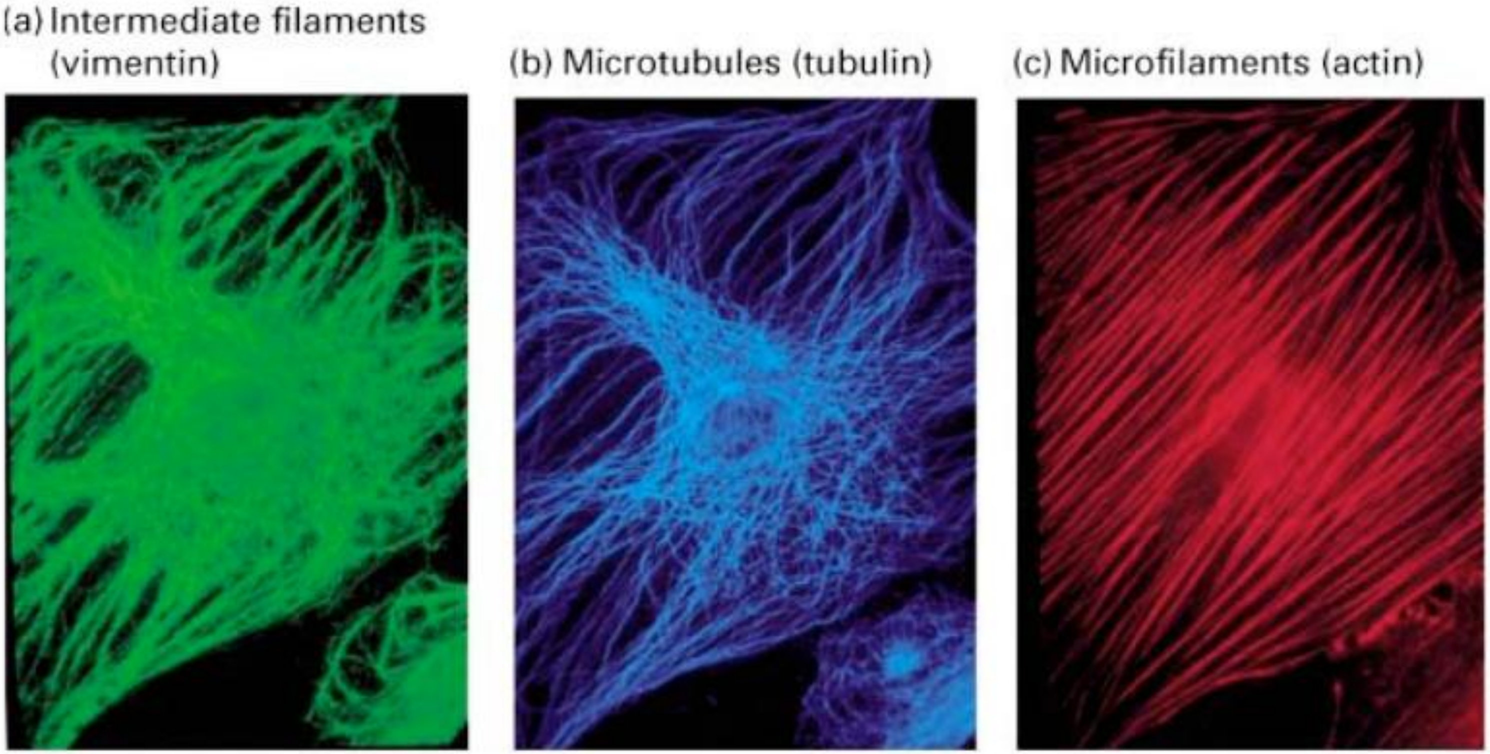


(b)



Introduction to Cell/Surface Interactions

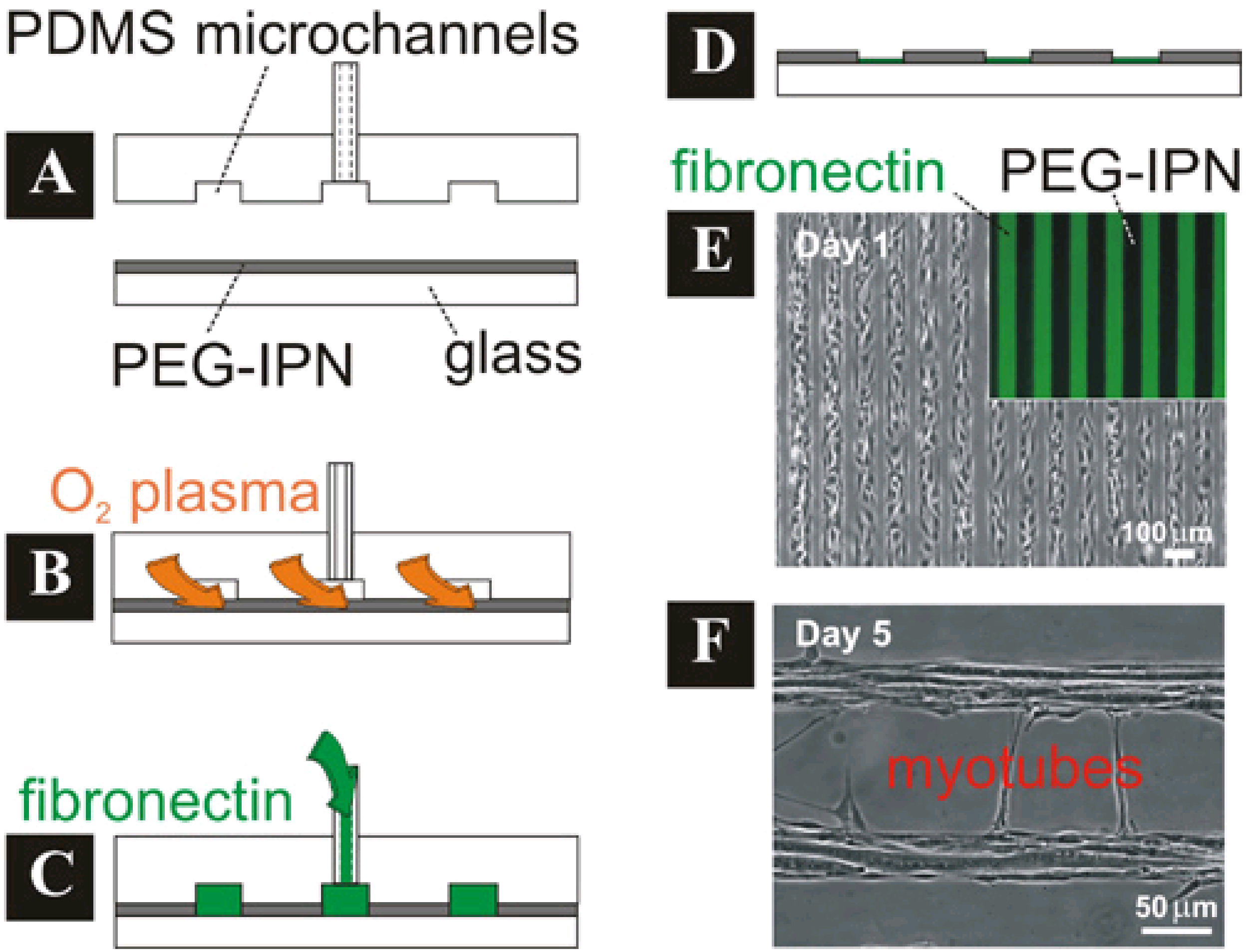
3 major cytoskeletal networks

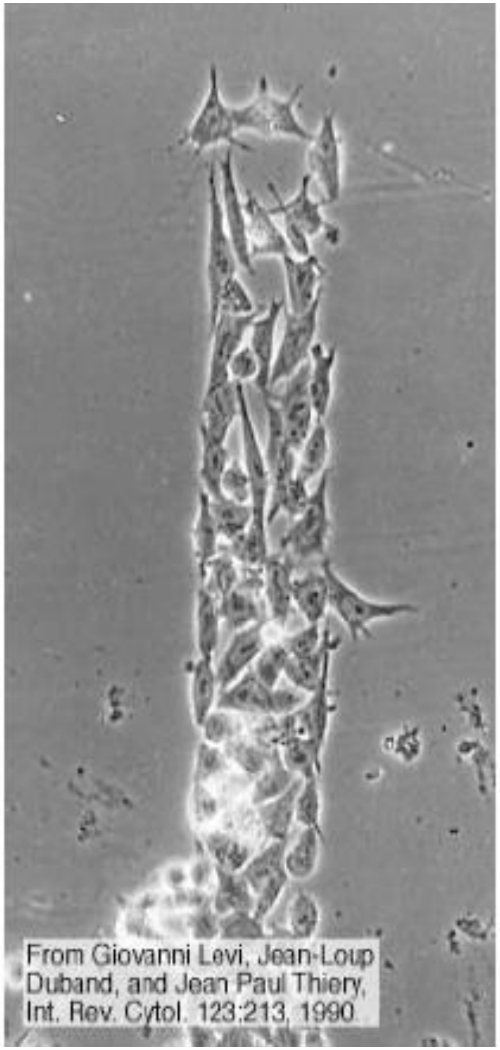


Lodish 19-50

Introduction to Cell/Surface Interactions

- Cells can be "tricked" into growing in a specific configuration using ECM proteins





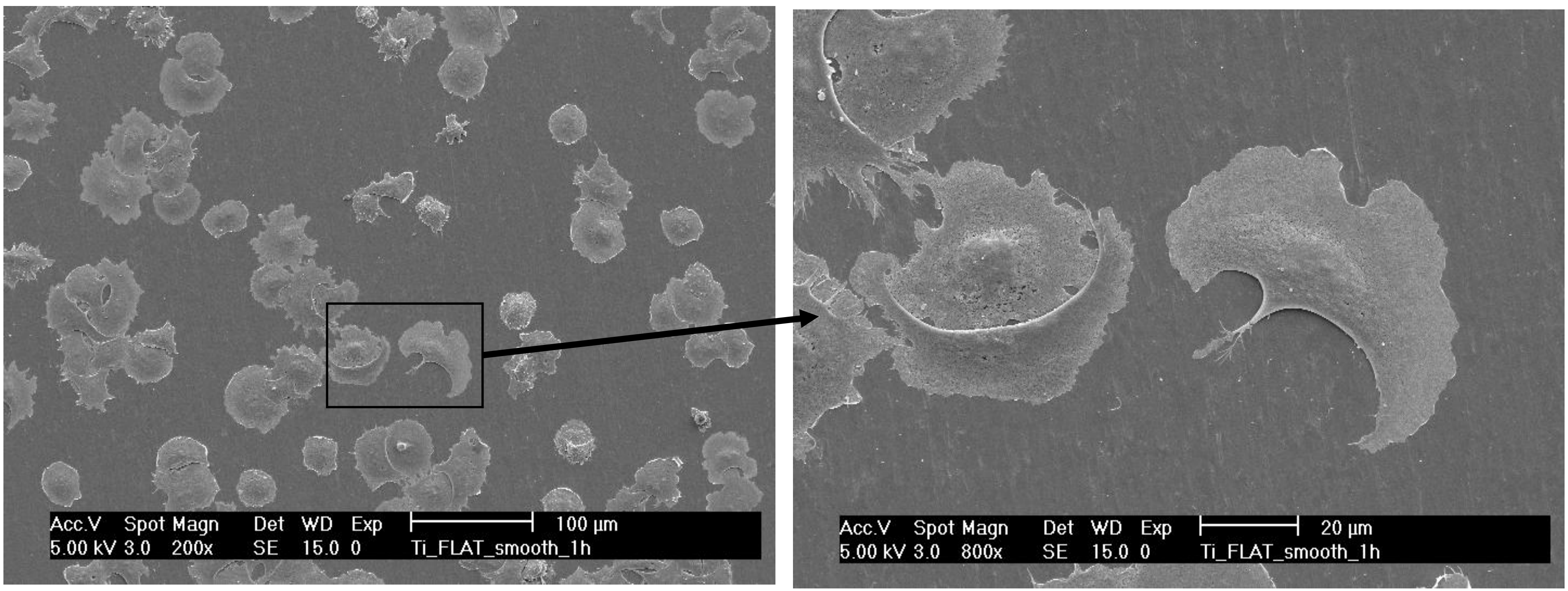
Fibroblast on collagen channel

Experimental Study of Cell / Surface Interactions

- Cell culture experiments on Ti-6Al-4V substrates
  - Polished surface
  - Different size grooves
    - Experiments done by J. Chen 2006, Soboyejo's group
- Goal of study:
  - Observe cell/surface interaction over a period of days
    - Analyze the influence of the surface on cell interaction
    - Look for evidence of "cell guidance"

SEM Views of Experimental Samples

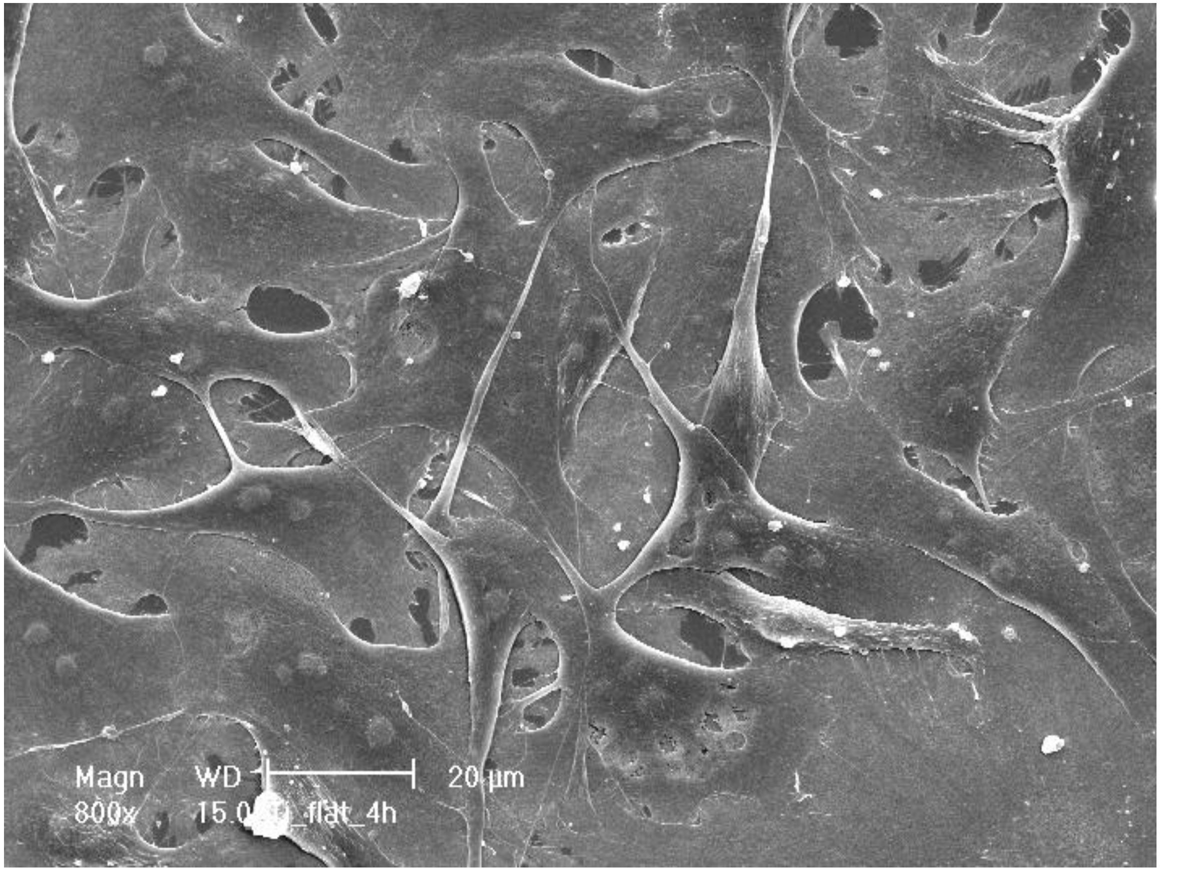
- Cell growth on polished surfaces after 6 hrs incubation
  - Cell exhibit random formations
  - No particular directionality of the cytoplast is observed



SEM Views of Experimental Samples

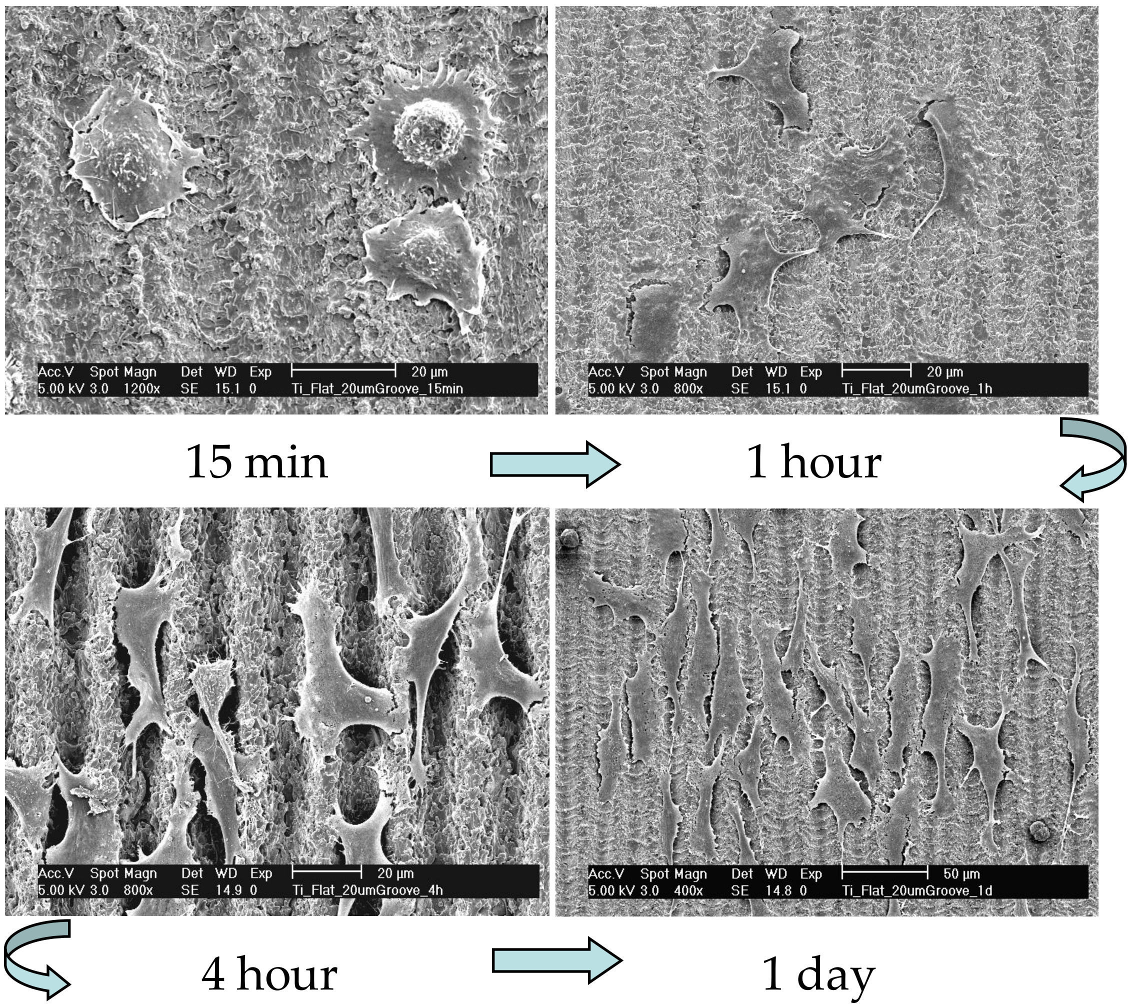
- Cell growth on polished surfaces after 48 hrs incubation

-Cell exhibit random cytoplasmic formations and no organizational pattern can be observed on the individual level
-Cells are arranged in multiple layers with multiple bridges between layers



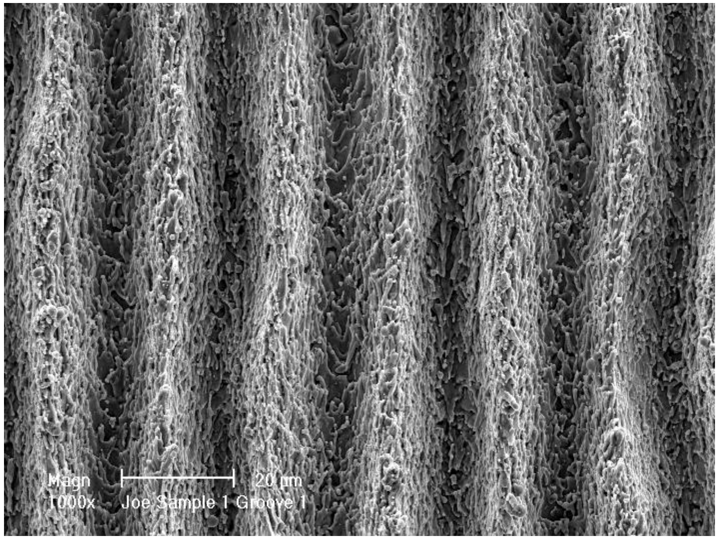
SEM Views of Experimental Samples

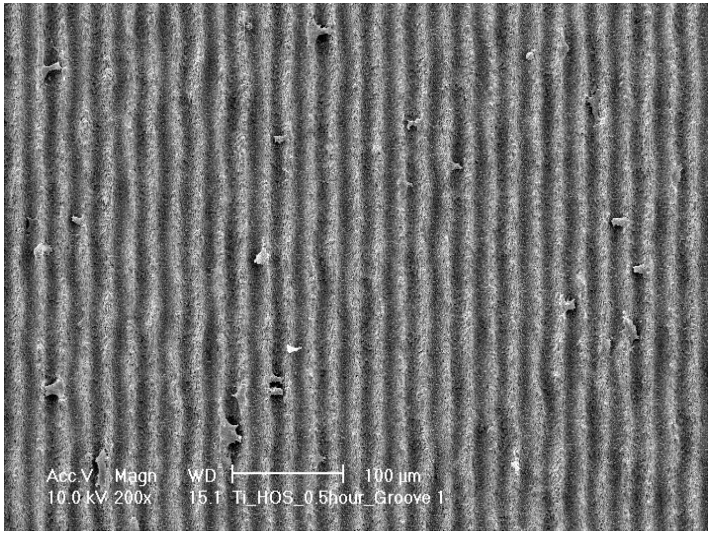
- Cell growth on grooved structures

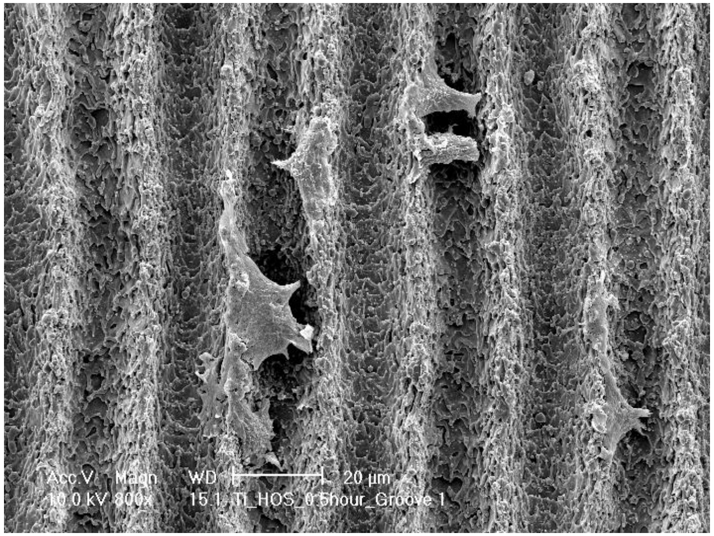


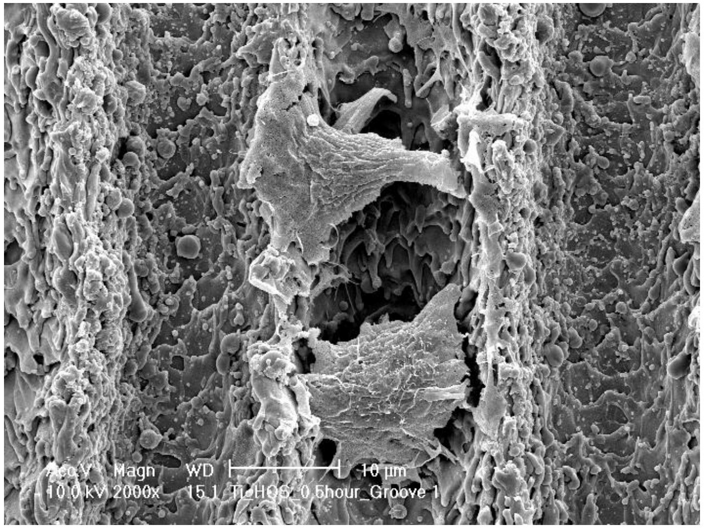
SEM Views of Experimental Samples

- Cell growth on grooved surfaces



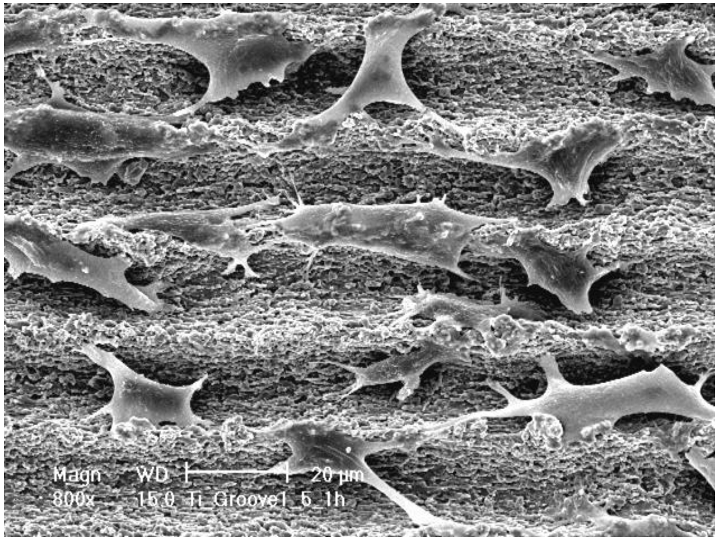


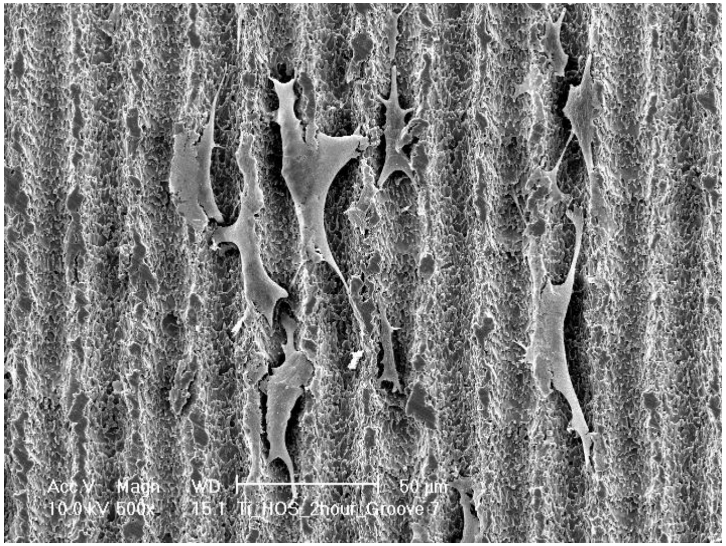


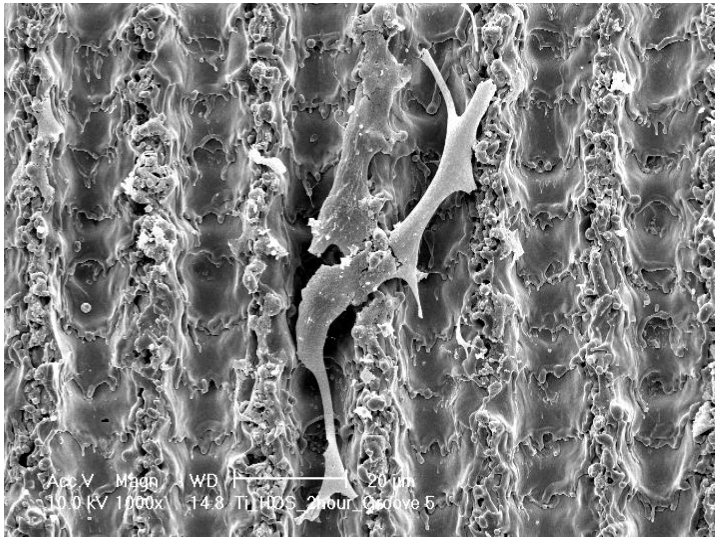


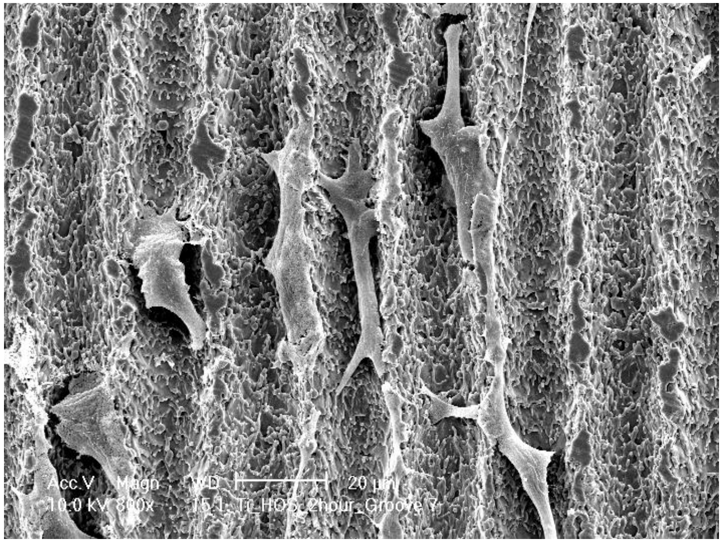
SEM Views of Experimental Samples

- Cell growth on grooved surfaces



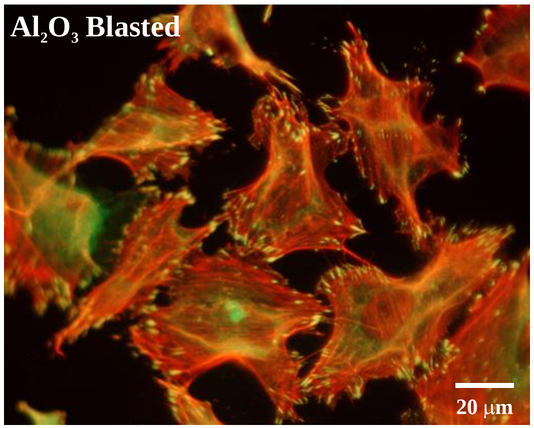


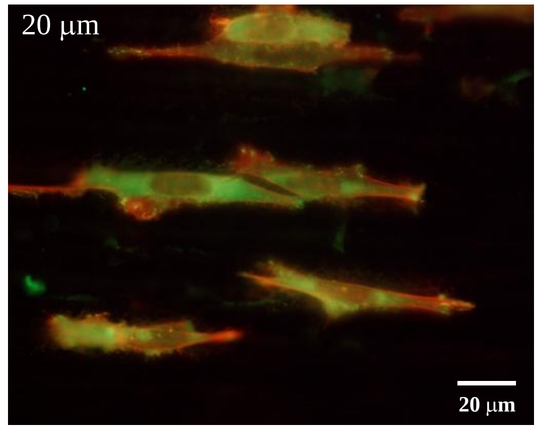


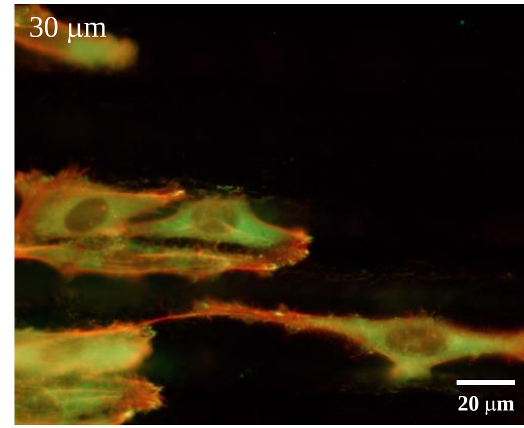


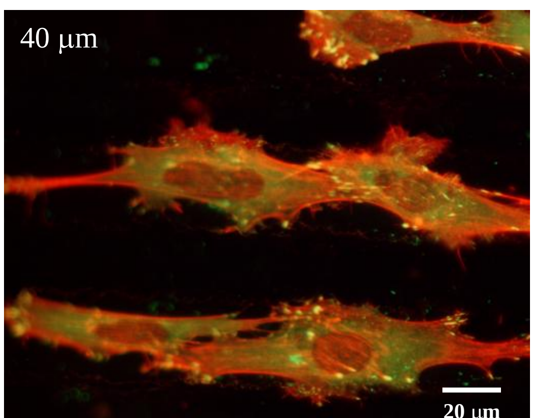
Confocal Views of Experimental Samples

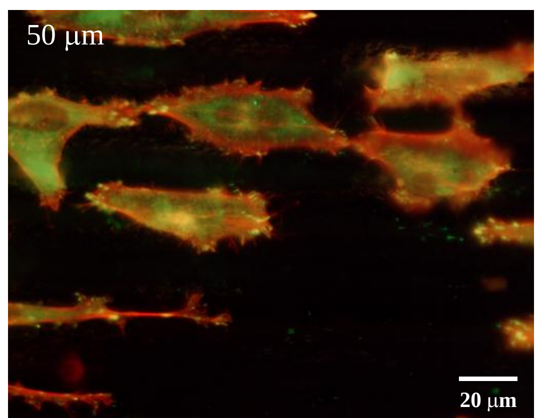
Green → Actin   Red → Vinculin

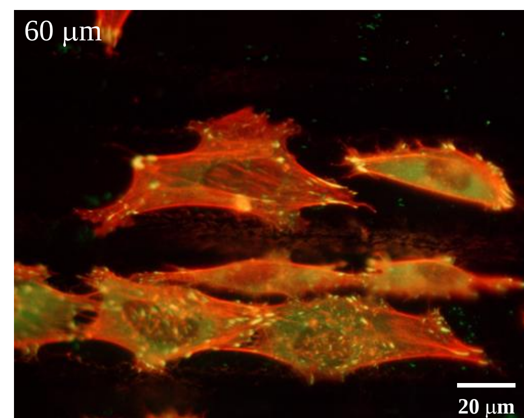










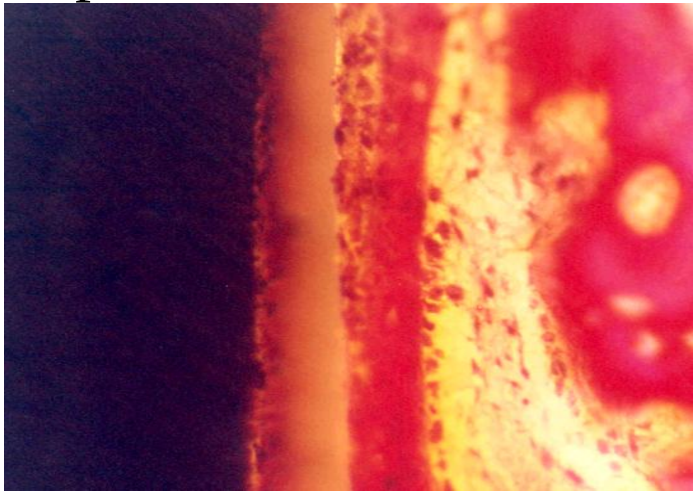


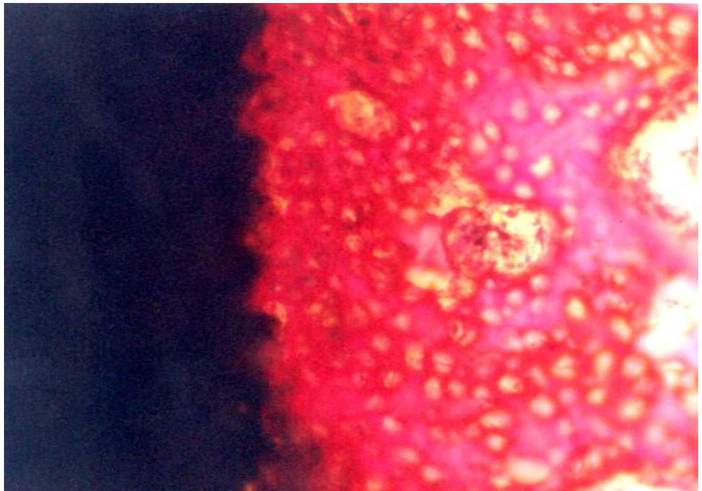
Summary of Cell/Surface Interaction Observation

- Contact guidance clearly occurs in the 10 to 40μm grooves
- Extensive spreading observed on smooth surfaces – almost complete coverage after a few days but in sheet like manner
  - No evidence of contract guidance!

Osteogenic Titanium Biomedical Systems

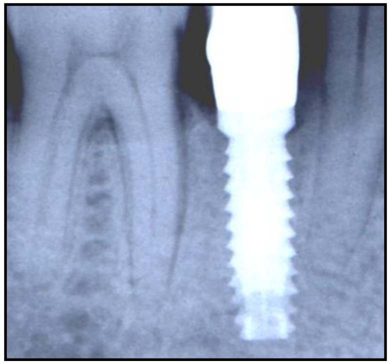
- An estimated 8-10 % of Americans have orthopedic implants - have a limited lifespan

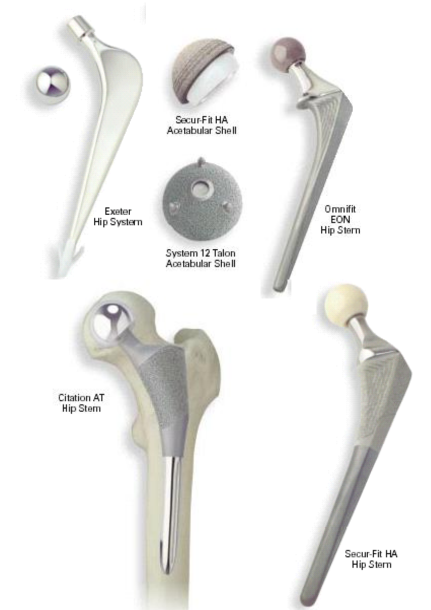




Implant Innovations, Inc.

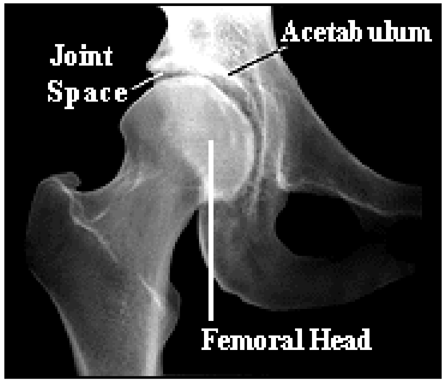
Dental Implants





Stryker Howmedica Osteonics

Hip Implants



Implications of Cell/Surface Studies for Implants

- Surface texture on implants can be used to template cell/tissue orientation
  - Could promote tissue-implant integration
  - Could limit scar tissue formation
- Surface texture can be used to control cell/surface adhesion
- Surface texture of implant could lead to greater adhesion and thus improve durability and life time of:
  - Hip and knee implants
  - Dental implants