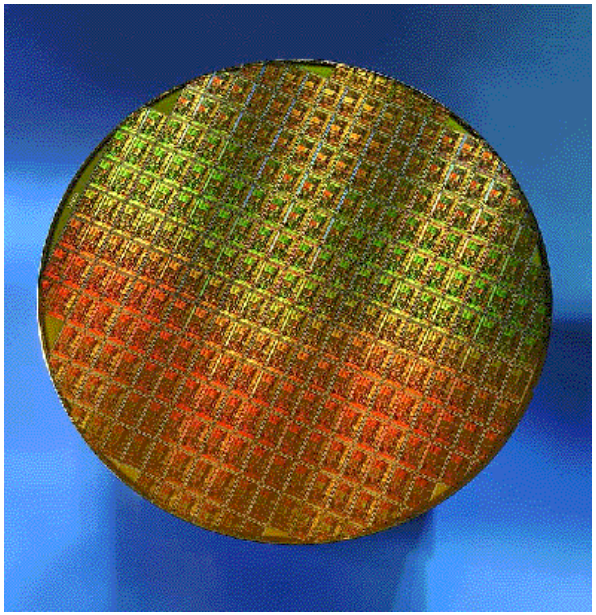
BioMEMs
Micro and Nano Fabrication

Biological Micro Electro-
Mechanical systems

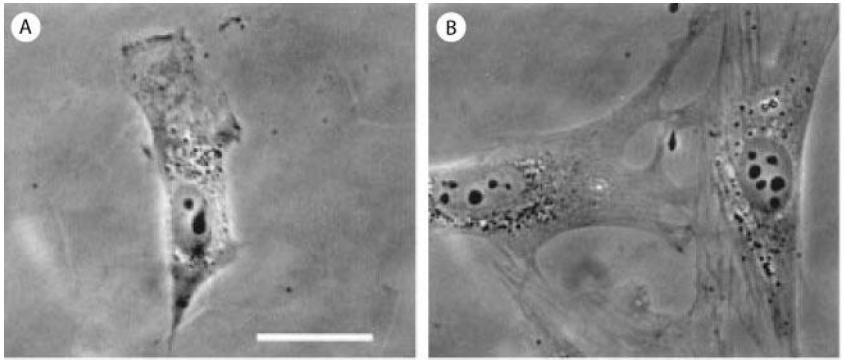
BioMEMs & Microfabrication

- Techniques from electronics field
  - Computer chips
  - Mini-sensors: pressure, acceleration, etc…
- Measure cell forces
- Impart cell forces
- Microfluidics
- Total systems

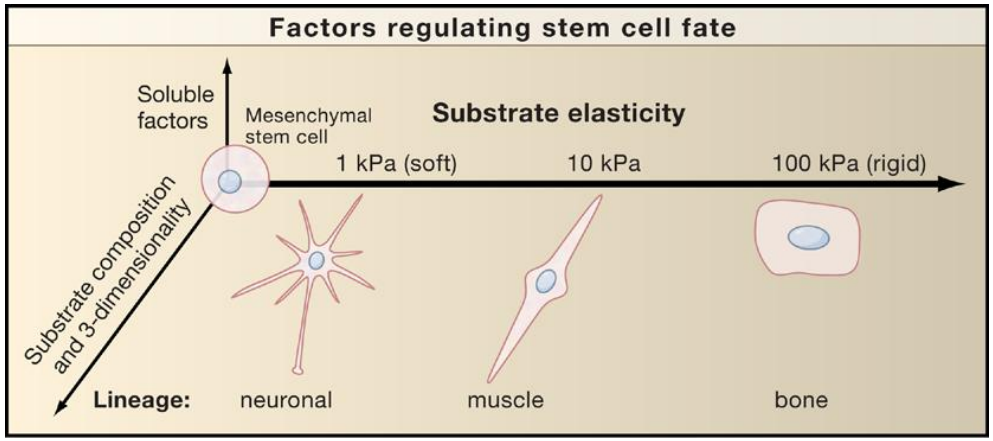


Mechanotransduction

- Cell Forces
  - Cell-Material Interactions
  - Cell-Cell Interactions
- Examine Cells
  - Develop measurement tools
  - Discovery of how cell parts interact with each other
- Cell stiffness response
  - (A) Soft PA .03% Bis
  - (B) Hard PA .26% Bis



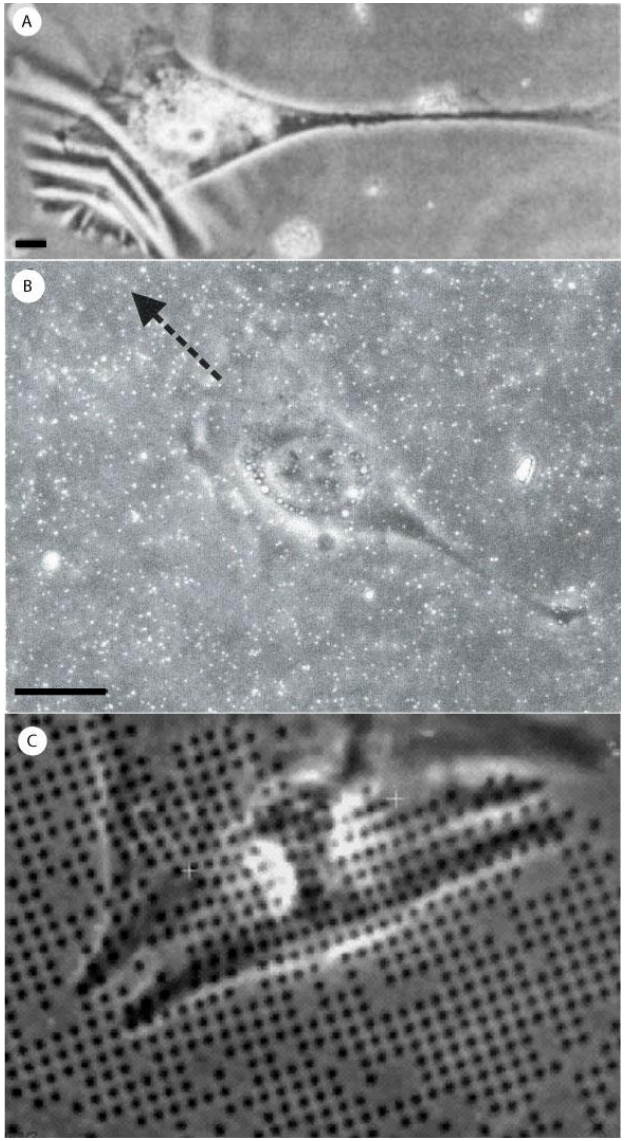
[Adapted from Pelham]



(Even-Ram, 2006 from Engler, 2006)

Measurement

- First detection: (A) Heat cured silicone membrane wrinkling
- Next breakthrough: (B) Traction force microscopy, bead displacement
- Refinement: (C) Patterned bead displacement
- Coupled displacements



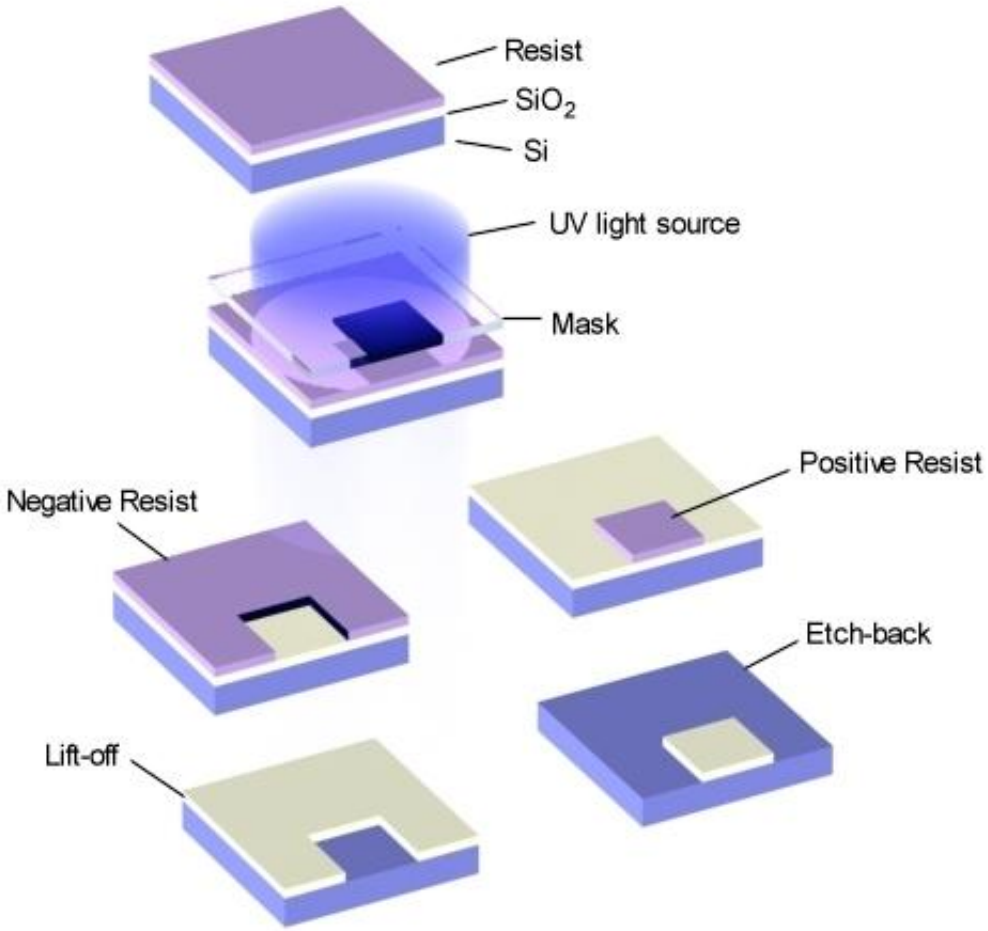
[Harris, Munevar, Balaban]

Lithography

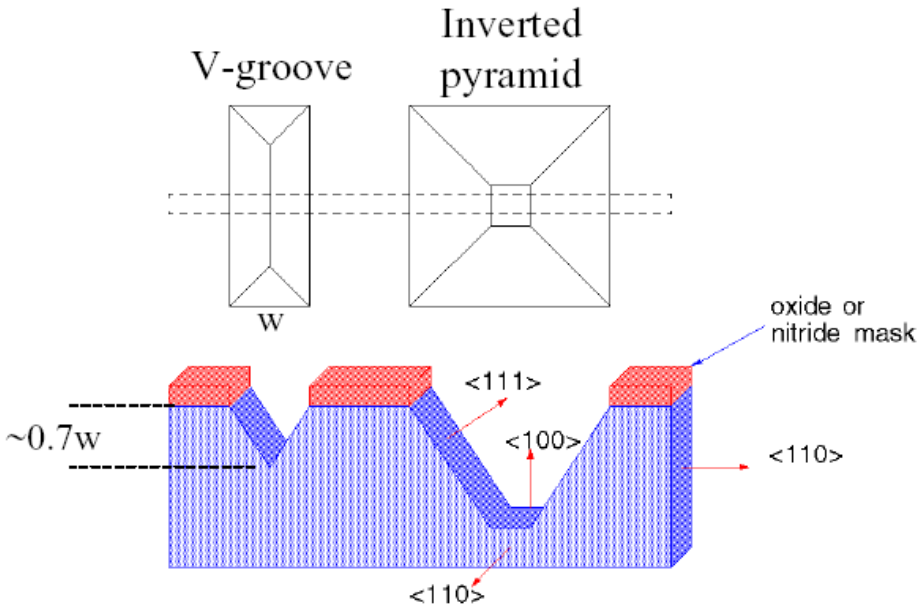
- Spin Photoresist
- Soft Bake
- Align Mask
- Expose
- Post Exposure Bake
- Develop

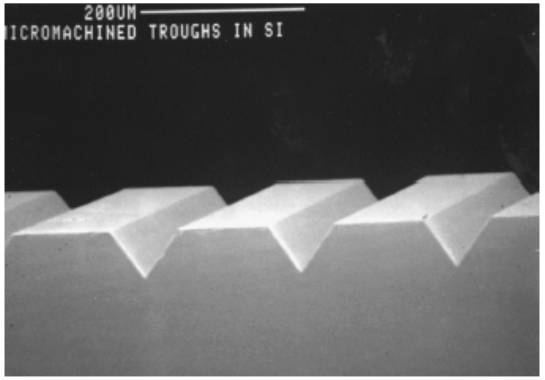
- Positive Resist:
  Photoactived compound becomes soluble in developer

- Negative Resist:
  Light causes resist to polymerize



Lithography – Bulk Micromaching

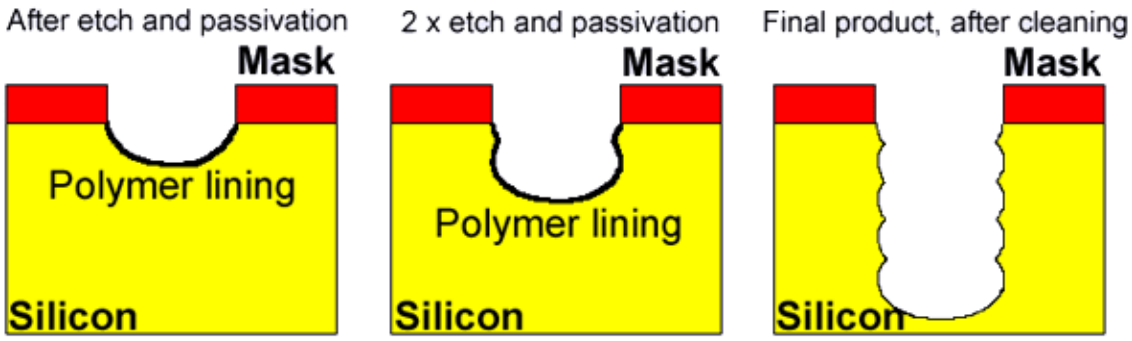




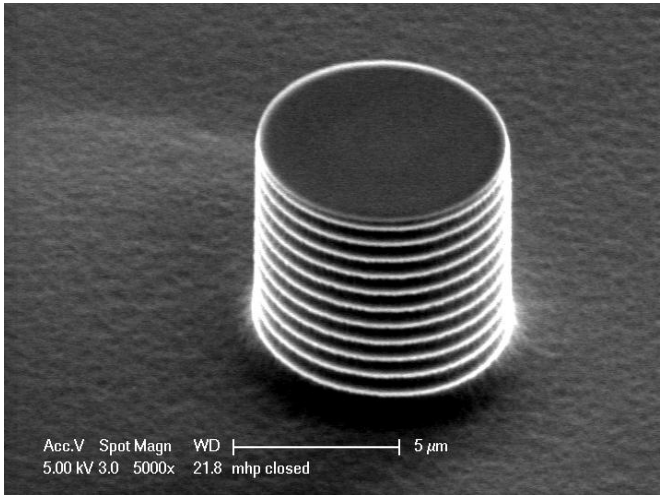
- Isotropic (universal direction) etch:
- XeF2 gas, HNA
- Anisotropic (directional per crystalline plane): KOH, ion etching

Lithography - Etching

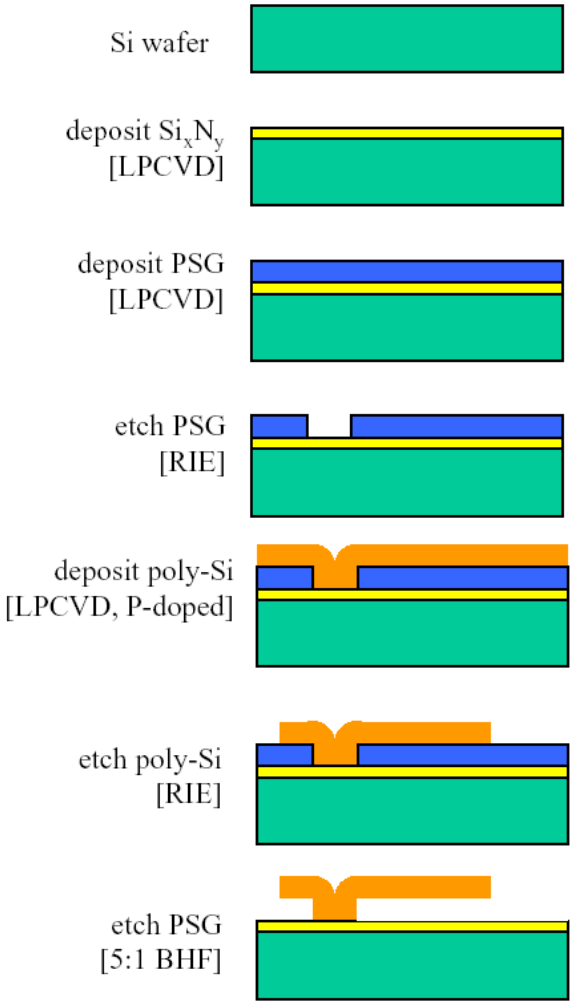
- Masks created using high-raster printers or direct write lasers
- ~100/50nm resolution for DUV/ExtremeDUV systems
- RIE, Deep-RIE

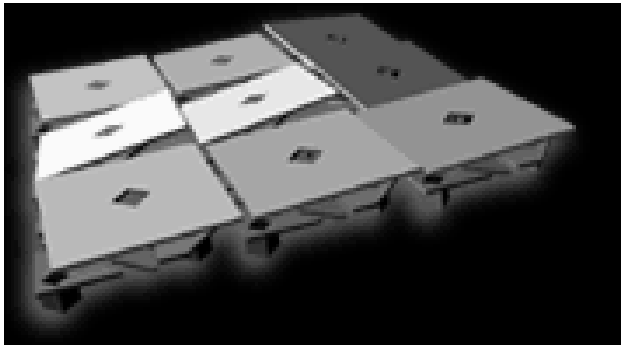


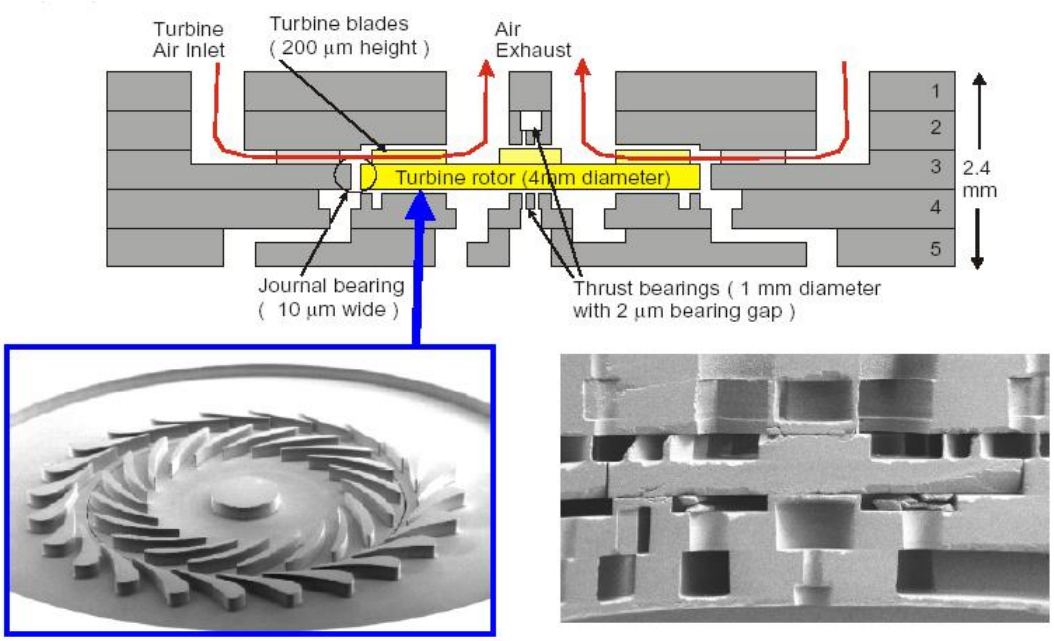
Etching (SF6 gas)
Passivation (C4F8 gas)



Feature Creation



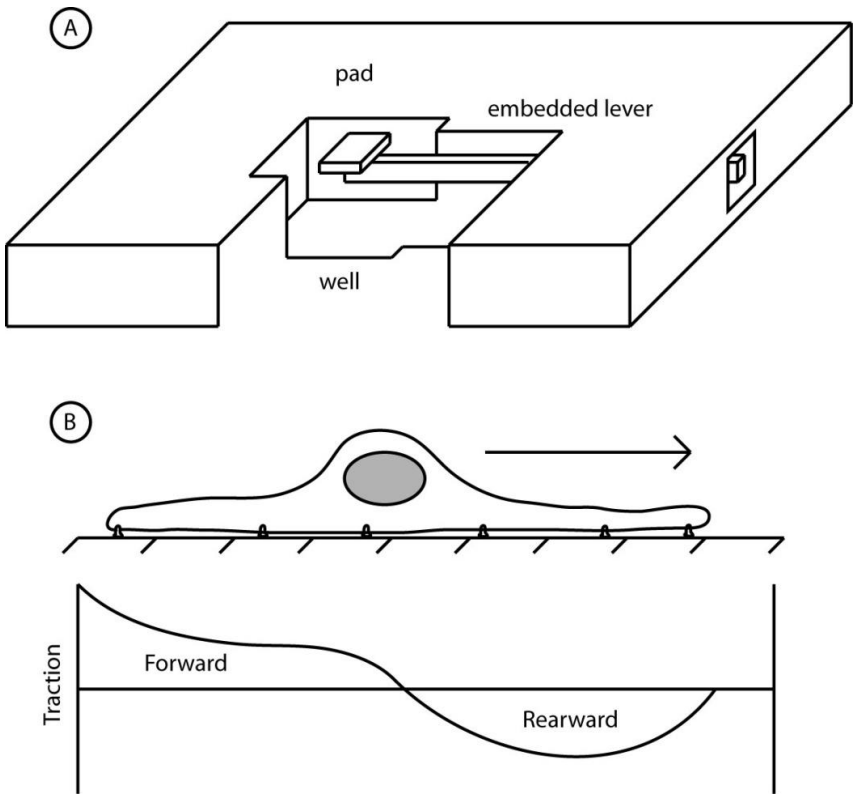




- Multiple layers can be stacked to create complex systems

Measurement

- MEMs cantilever in silicon
- (A) Horizontal displacement, with varying pad area
- (B) Discovers front of cell pulls, rear of cell pushes

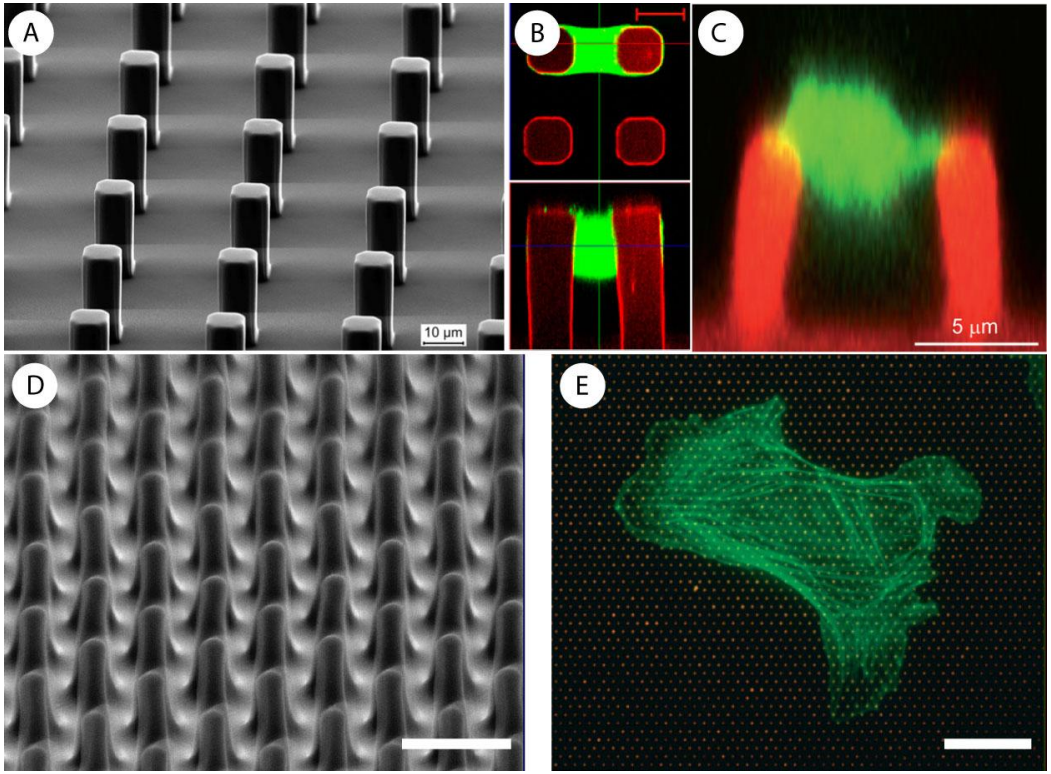


[Adapted from Galbraith]

Measurement

- Microposts
- (A) Megaposts:
- (B) cardiac myocytes
- (C) clumps of platelets

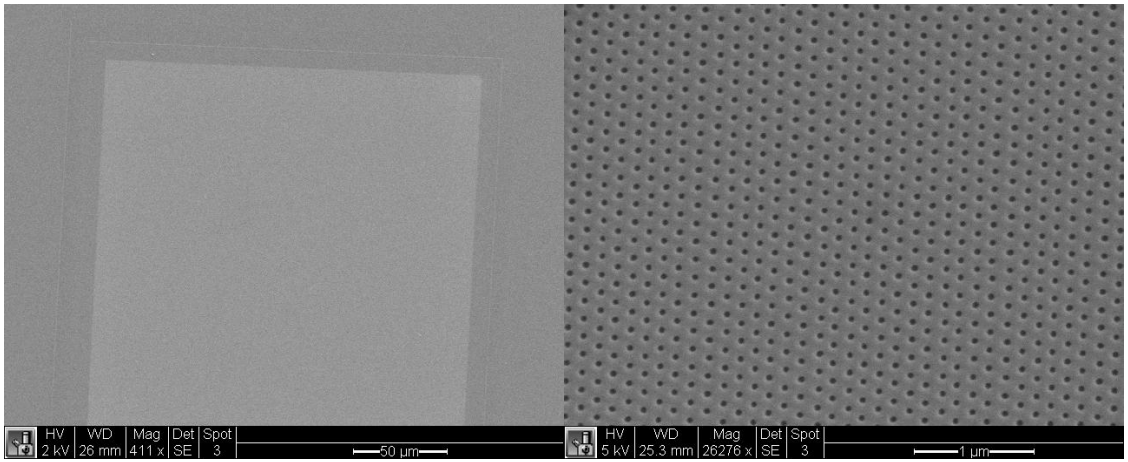
- (D) Nanoposts:
- (E) Higher precision



[Kajzar, Liang, Yang]

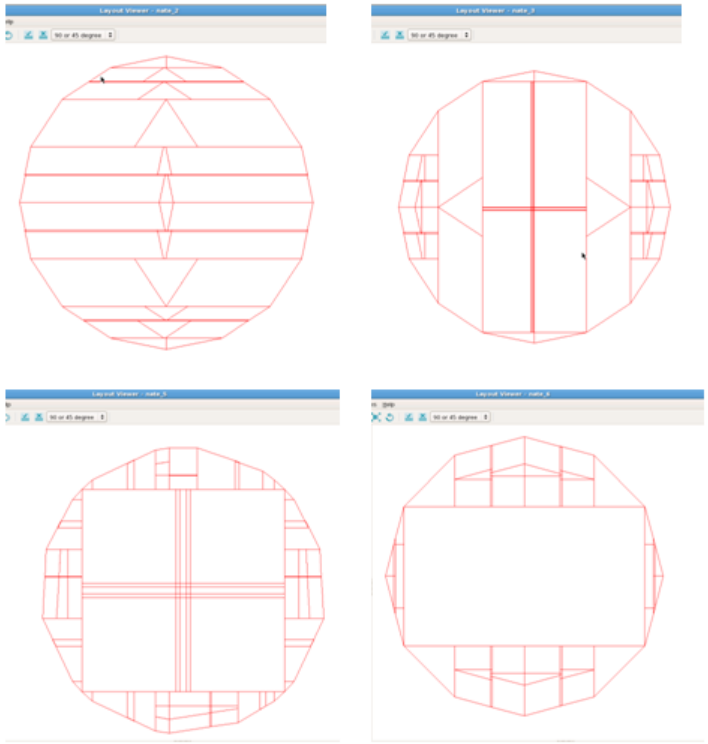
Electron Beam Lithography

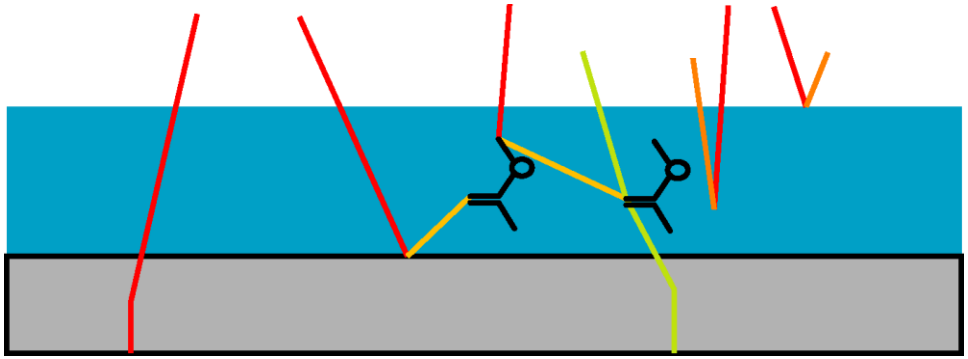
- JEOL JBX electron beam writer
  - Minimum field resolution: 1.25 angstroms
- Resolution is sensitive, special challenges
  - Temperature, humidity
  - Ground vibration
  - EM field noise
  - Special room



Electron Beam Lithography

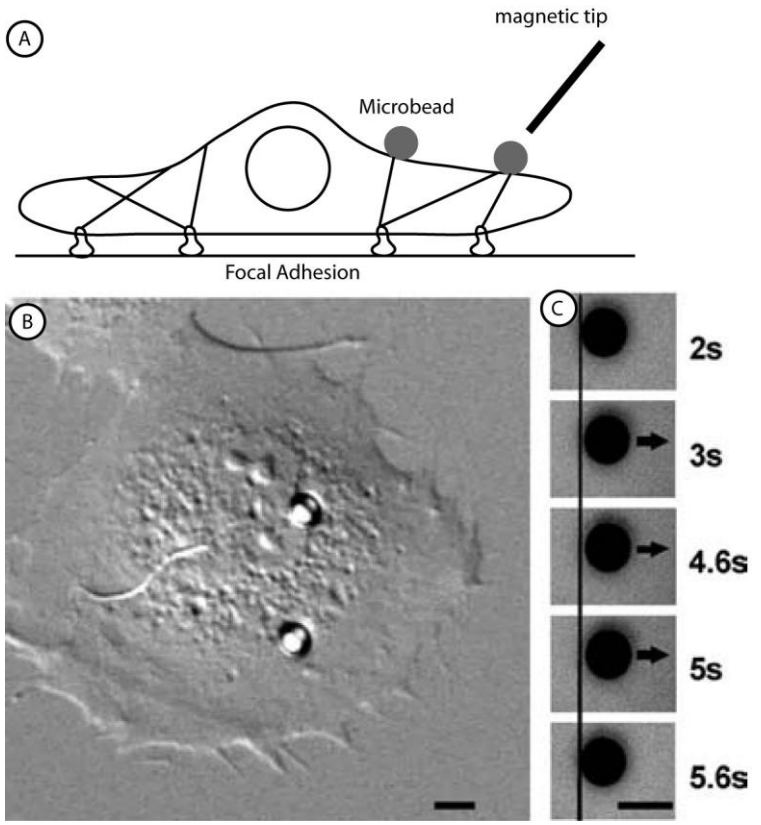
- Slow, but accurate writing.
- Like writing an image 1 pixel at a time
- Electron Scattering





Apply Force

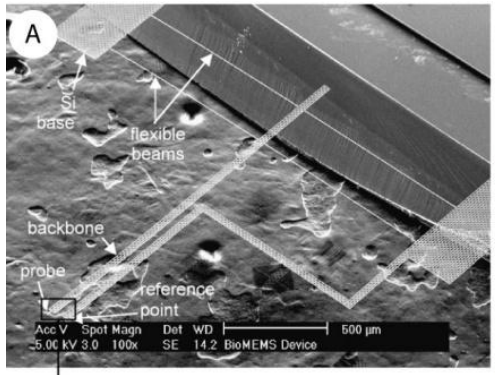
- Most basic: micromanipulator + pulled glass tips
- Magnetic twisting cytometry: (A) Adhere bead, (B-C) twist or pull on bead

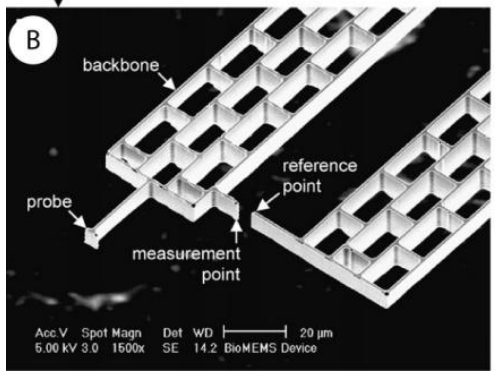


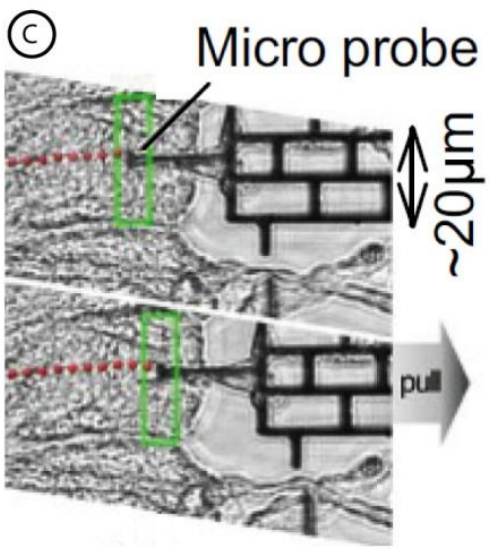
[Adapted from Matthews]

Apply Force

- MEMs cantilever in silicon
- Expansion of glass needle concept
- Incorporates reference point during pulling, better accuracy

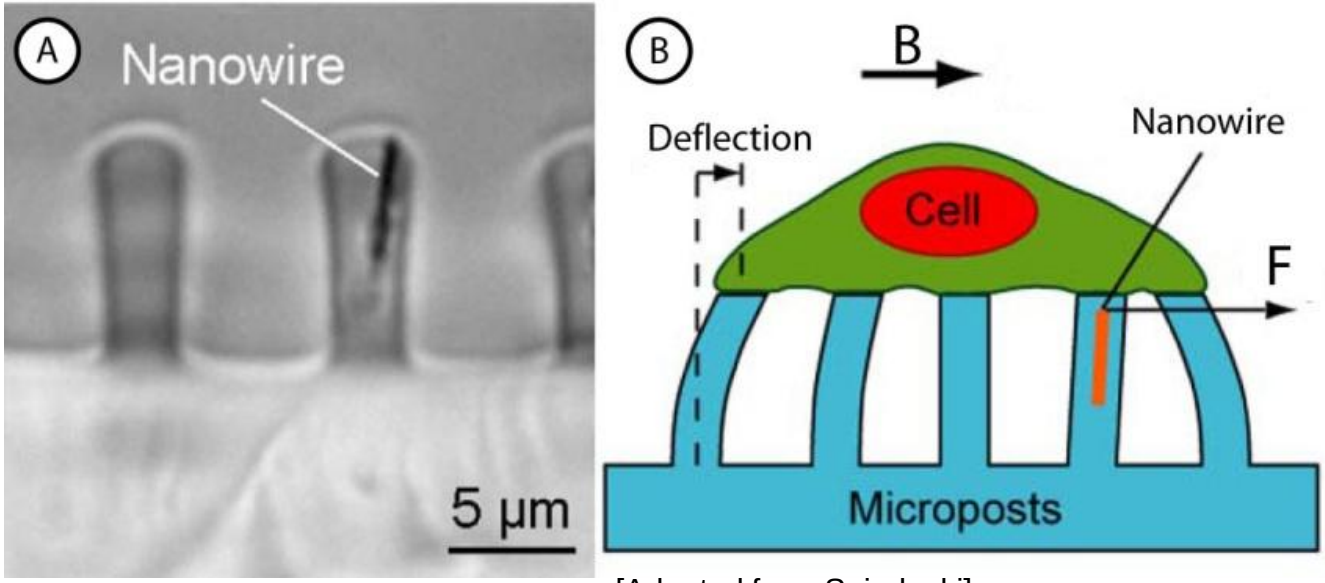






[Adapted from Yang]

Apply Force

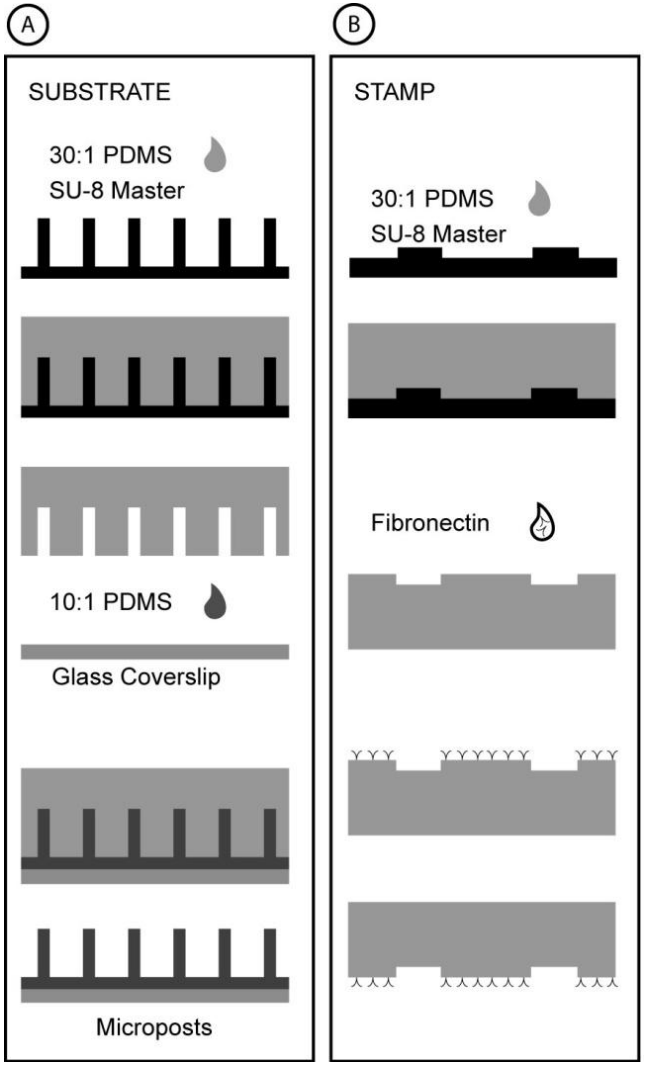


[Adapted from Sniadecki]

- Magnetic microposts
- Embedded ferromagnetic wire
- Global field applied

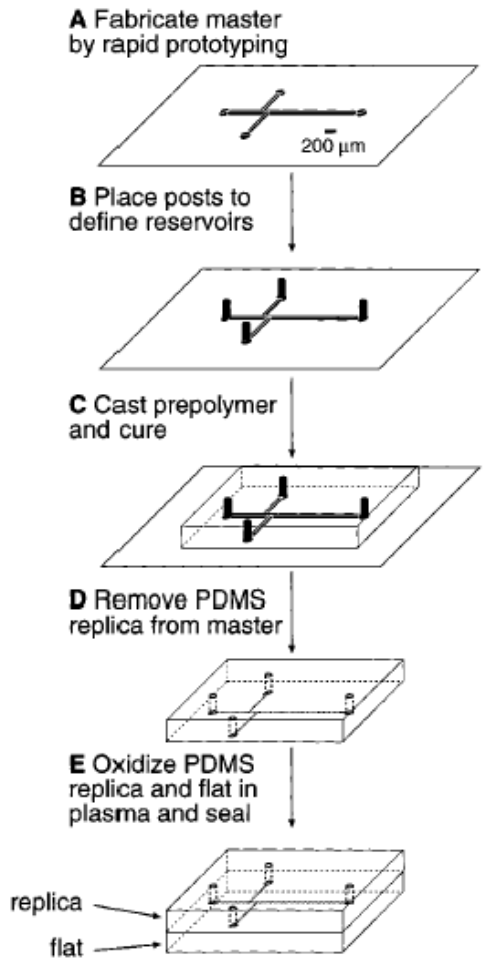
- Apply local force, see whole cell response simultaneously

Soft Lithography – Polymer Replication



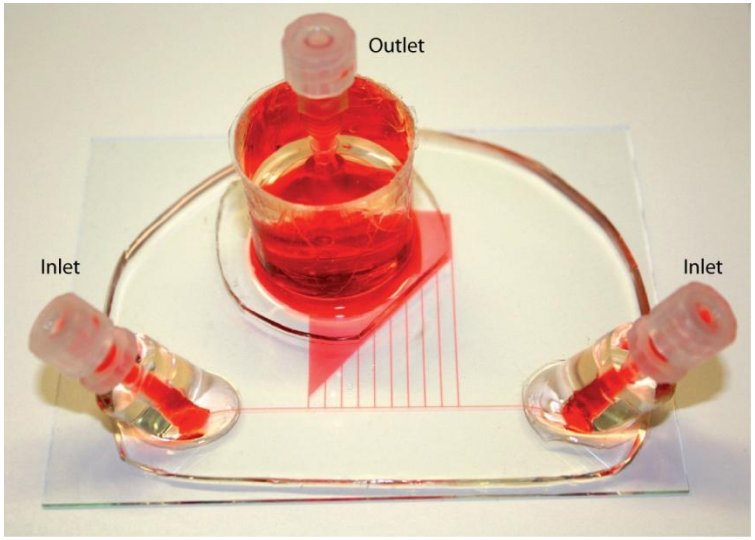
- (A) Features are created in silicon or photoresist, a negative is cast, then a positive is case
- (B) Negative features are created, then a positive is cast

Microfluidics



Duffy et al. 1998

- Shear forces for cells
- Many variations, single channel, multi channel, channel + stretch, channel + microposts, etc…

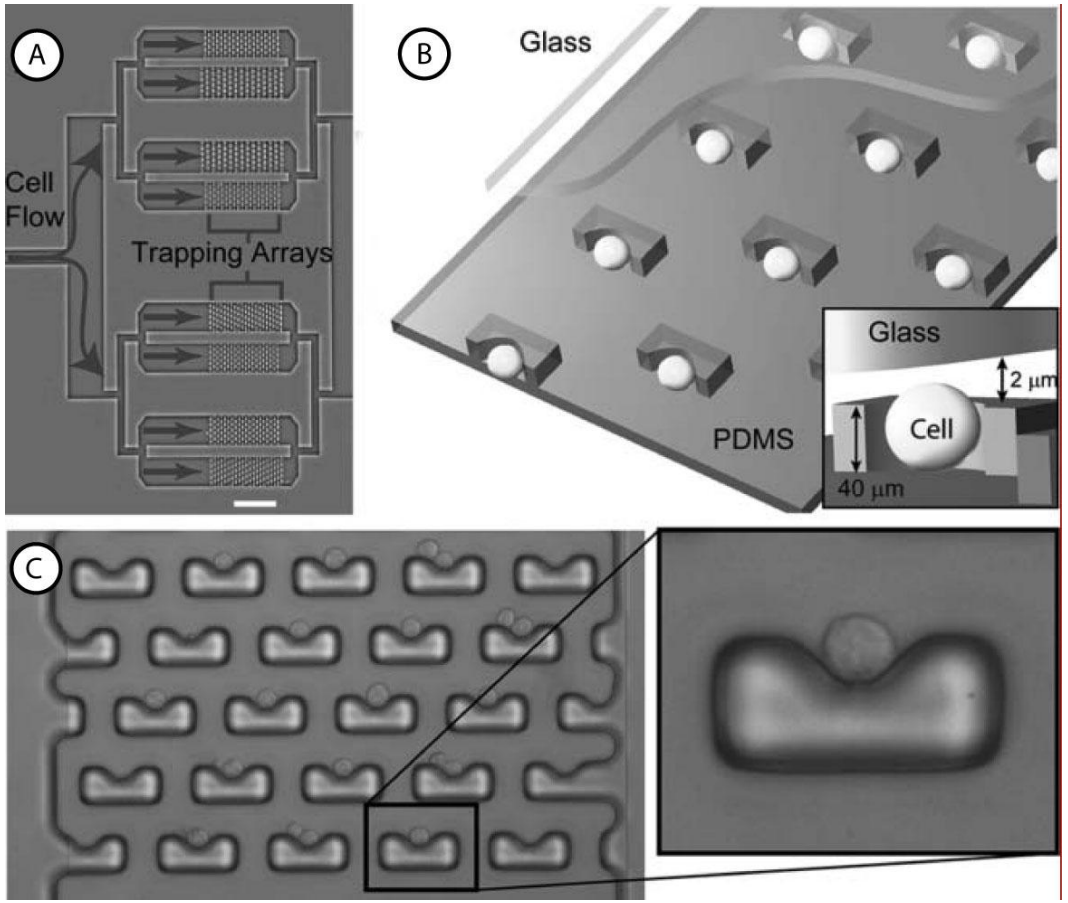


[Adapted from chau]

Microfluidics

- Single cell sorting
- (A) flow setup
- (B) channel setup
- (C) a single cell

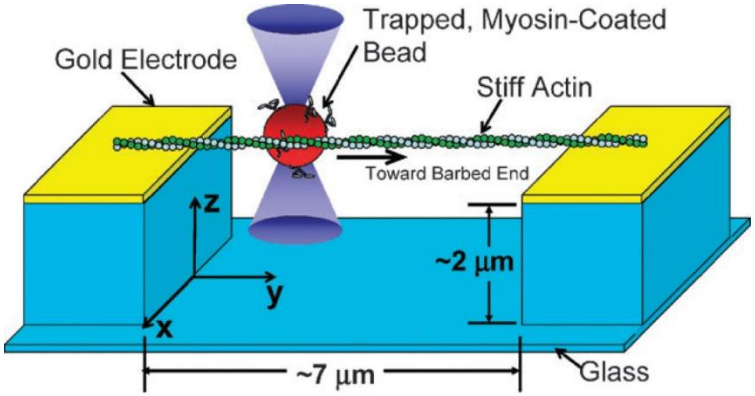
- Why single cell?
  - If you measure behavior through averages, you can miss modal behaviors



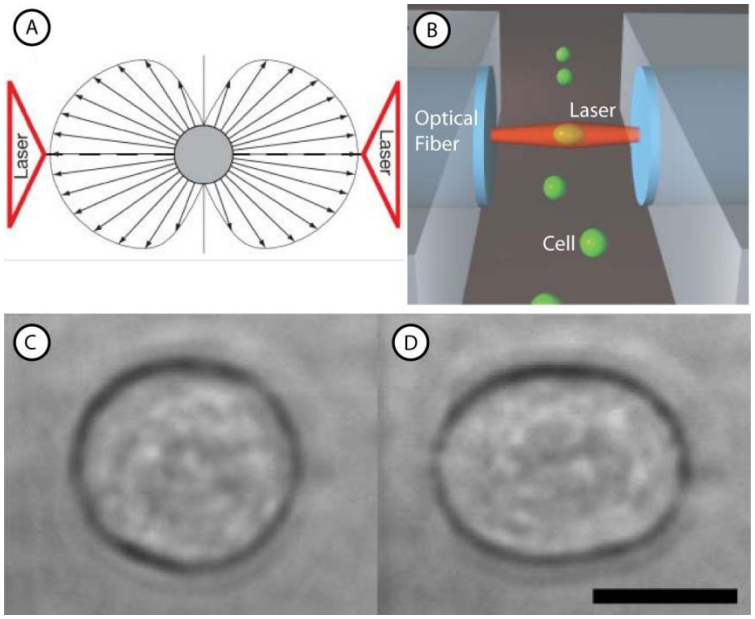
[Adapted from Di Carlo]

Apply Force /w Microfluidics and Optics

- Optical traps, tweezers can manipulate beads on cells, proteins
- Stretch cells without contact with (A) divergent beams, (B) sort in microfluidics, (C) unstretched (D) stretched
- Check non-adherent cell properties



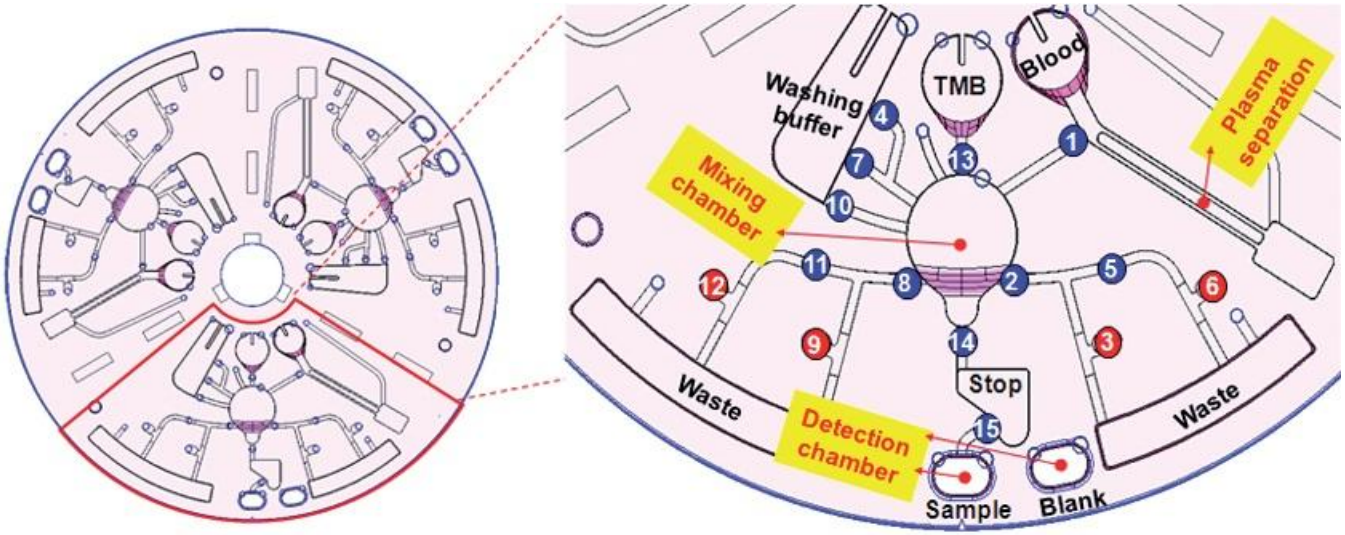
[Adapted from Arsenault]



[Adapted from Guck]

Microfluidics – Lab on Disc

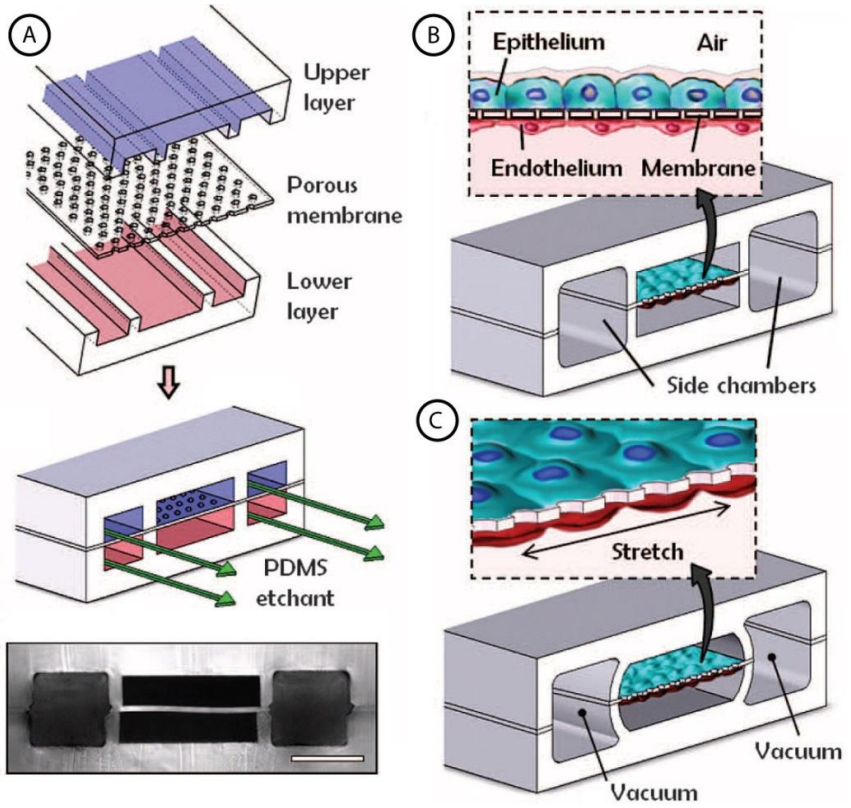
- Lab on chip / Lab on disc assays for high throughput detection of biomarkers
- In this example, ELISA immunoassay for hepatitis (Enzyme-linked immunosorbent assay)



[Adapted from Lee]

Microfluidics – Organ on Chip

- Organ on chip: Lung
- (A) Construction
- (B) Dual cells on PDMS membrane
- (C) Stretch and chemical exchange



[Adapted from Huh]

Questions?

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