Session 25

MECHANISMS OF MECHANOTRANSDUCTION

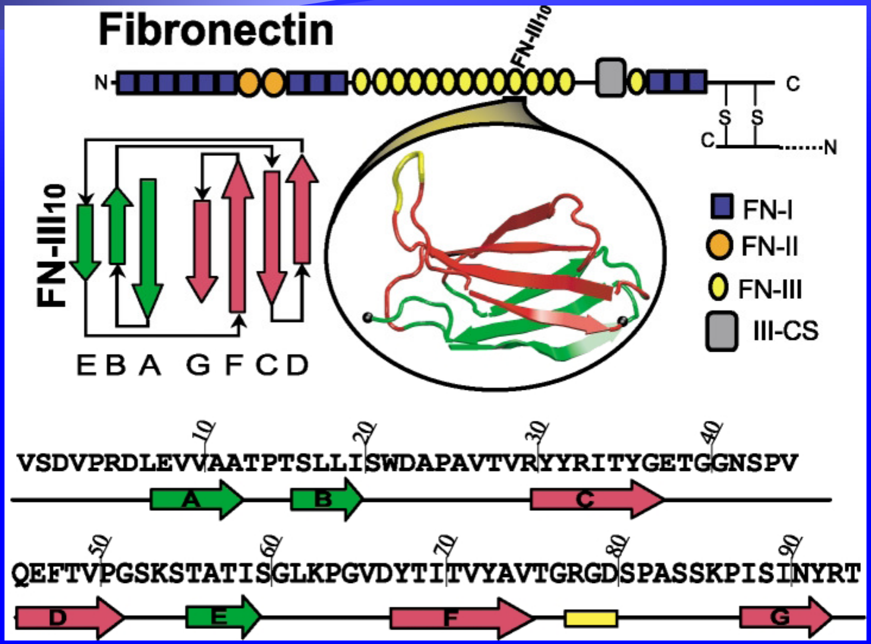
Generalized Mechanotransduction

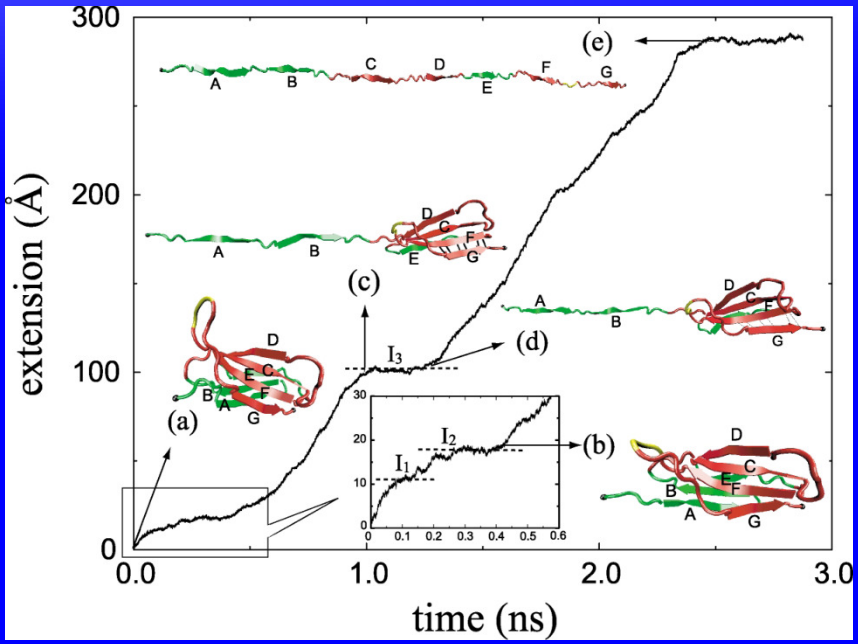
- Cell function defined by cycles
  - Mechanosensation
  - Mechanotransduction
  - Mechanoresponse

- Feedback in Response
  - Initially, many signaling pathways can be activated
  - Signals integrate to control cellular functional response
  - If response is "mechanical" (migration, contraction, etc.)
  - Elicit 2nd cycle of mechanotransduction

Exposed Cryptic Domains

- CSK and ECM proteins have tandem-repeated sequences

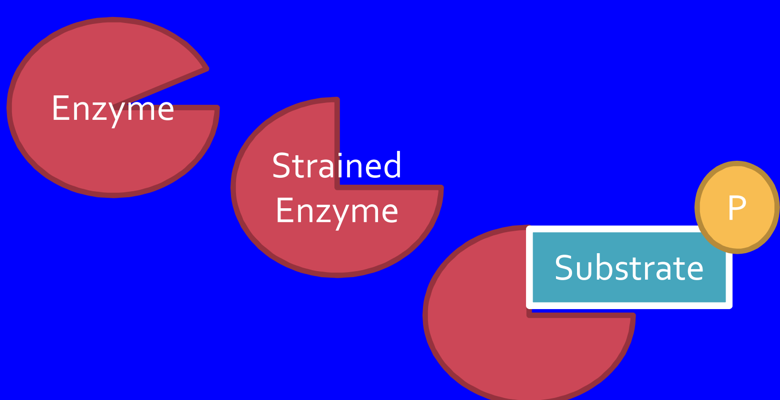


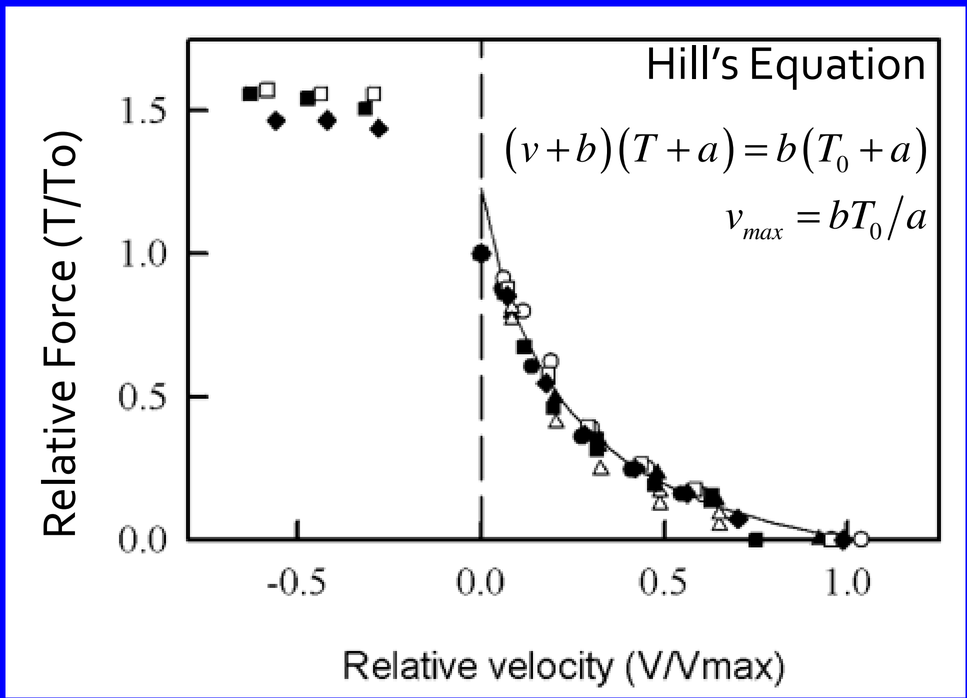


- Force induces unraveling of proteins
  - H+ bonds define tertiary structure
  - Mechanical stability depends upon frequency of H2O interactions
  - Amino acid side chains can shield H+ bonds

Force-Regulated Protein Activity

- Force could be potent regulator of enzymes
- Example: decreased Myosin ATPase turnover with increased tension
- Could conformation strains increase activity of some enzymes?

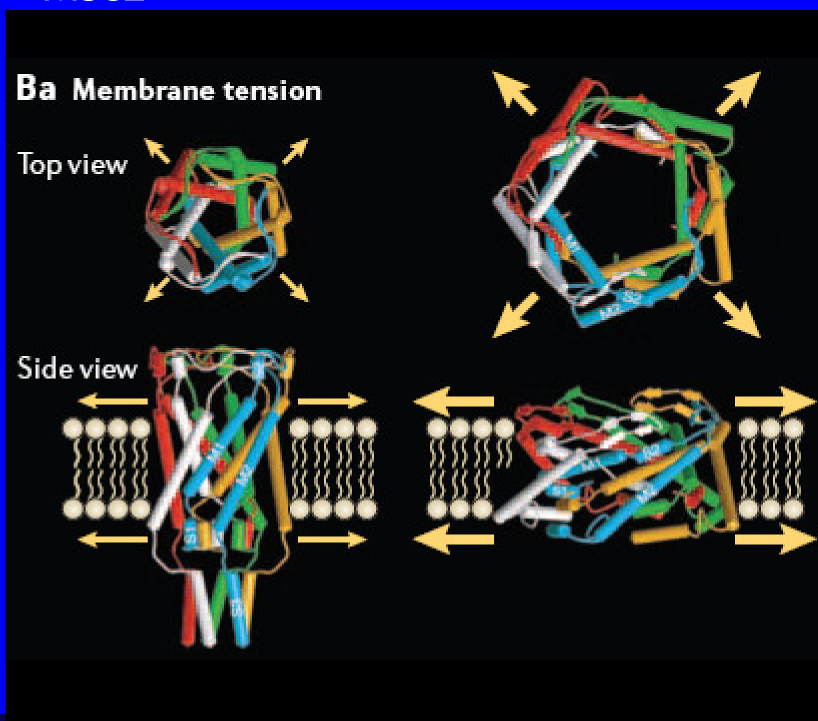




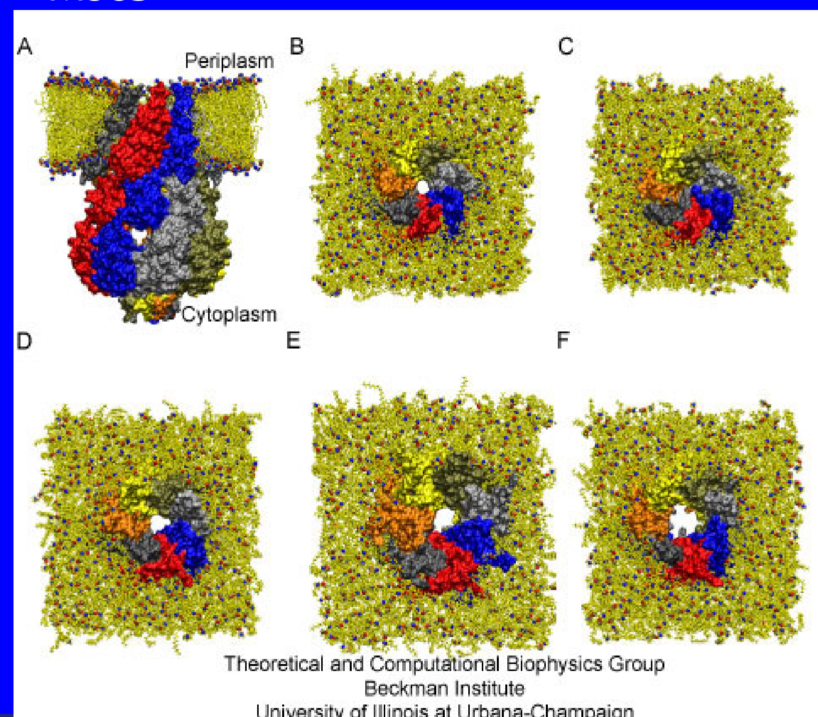
Mechanosensitive Ion Channels

- Stretch ion channels are a physiological necessity
  - Safety valve in bacteria to large forces
  - Mechanosensor in eukaryotic cells to small forces

MscL



MscS

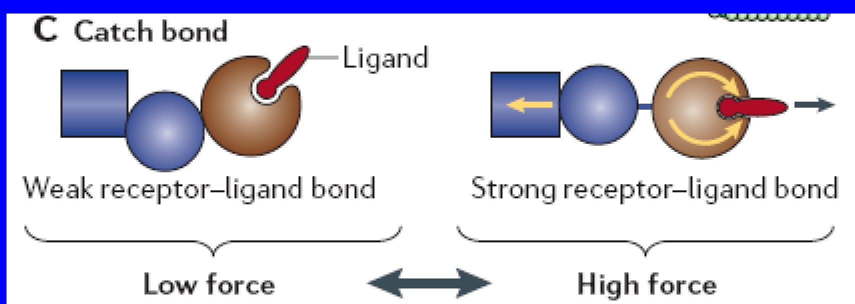


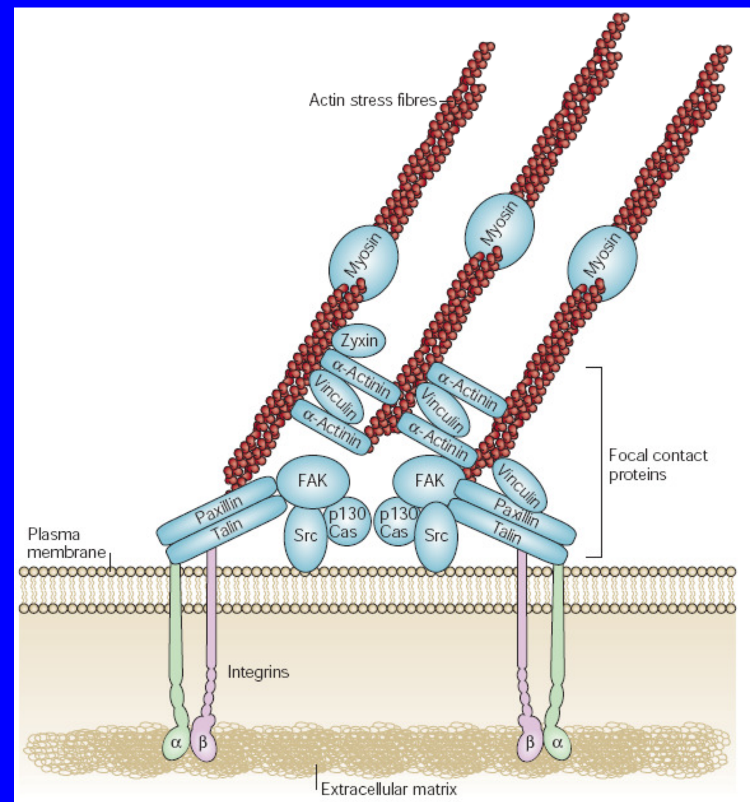
Slip Bonds/Catch Bonds

Biotin-Avidin *(strongest non-covalent bond)*

Force	Lifetime
0	1 day
5 pN	1 min
170 pN	1 msec

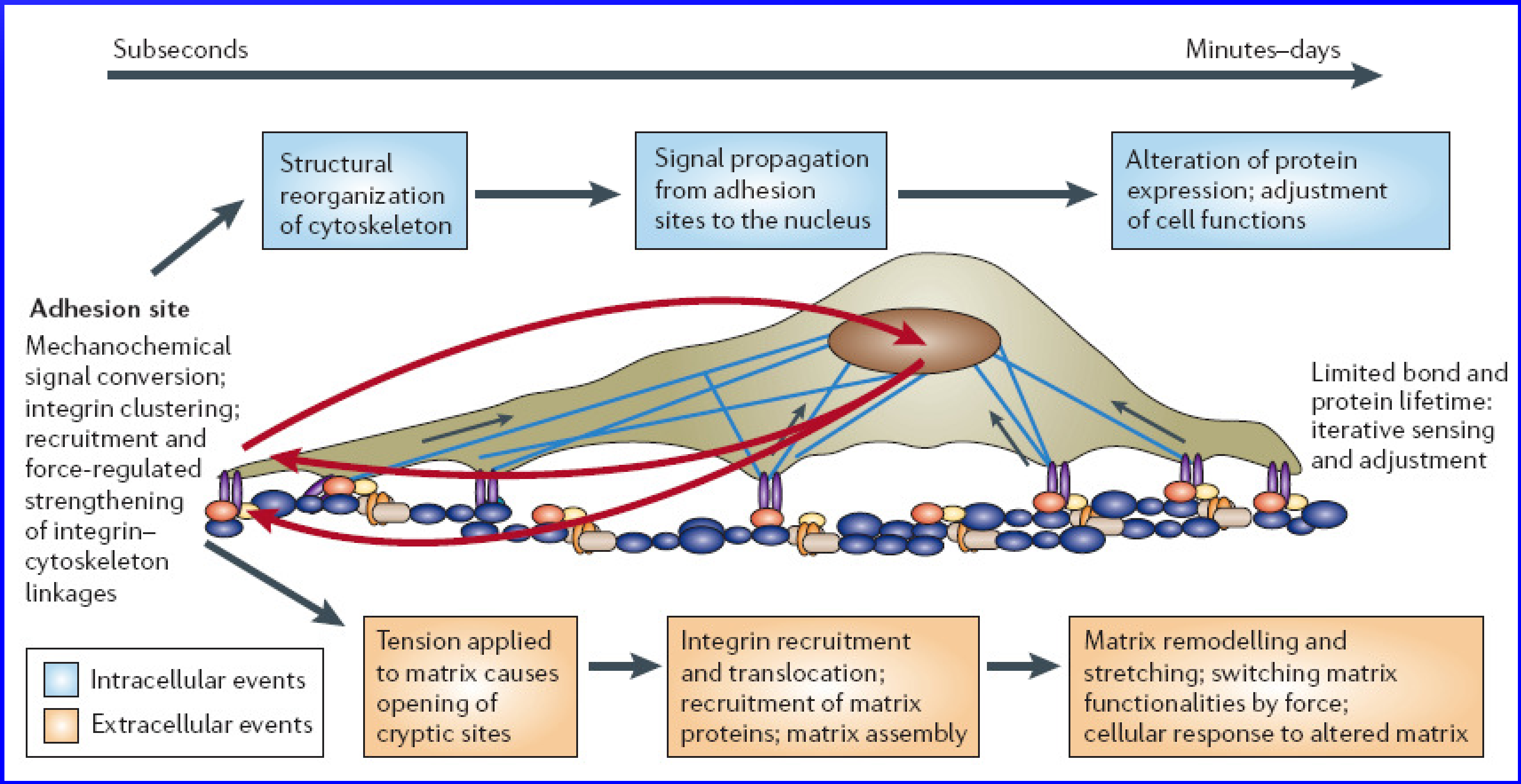
- Slip bonds: force-*reduced* average lifetimes
  - Focal adhesions under tension have high protein turnover
  - Sustained adhesion possible through integrin clustering
- Catch bonds: force-*enhanced* average lifetimes





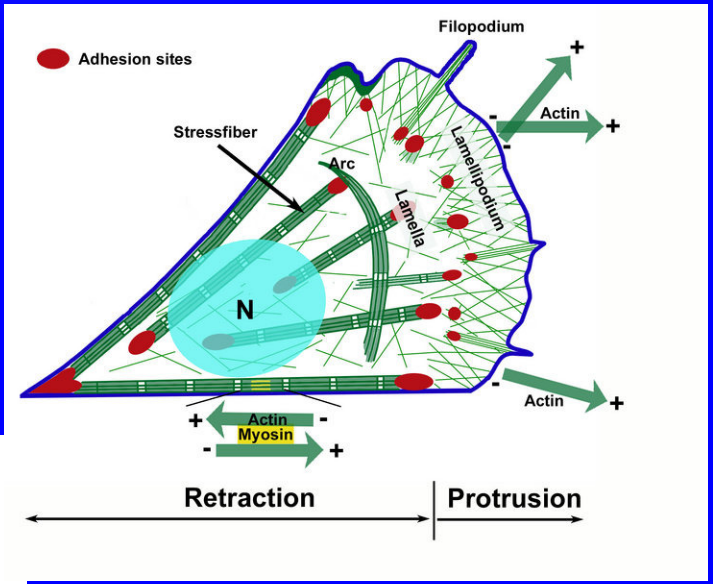
Internal and External Influences

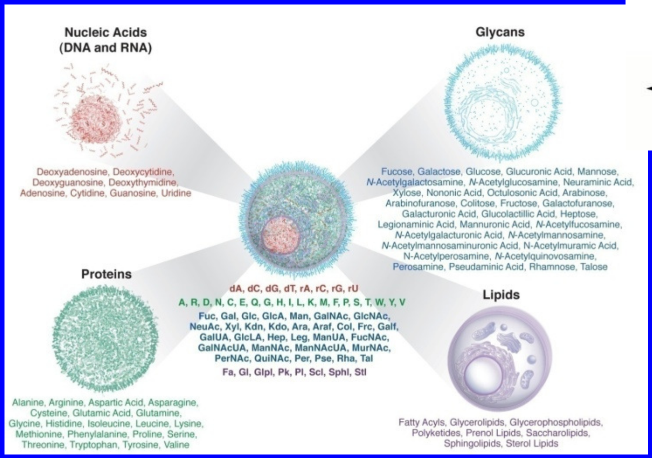
- Mechanosensing over time involves periodic changes and responses



Review of ME599F

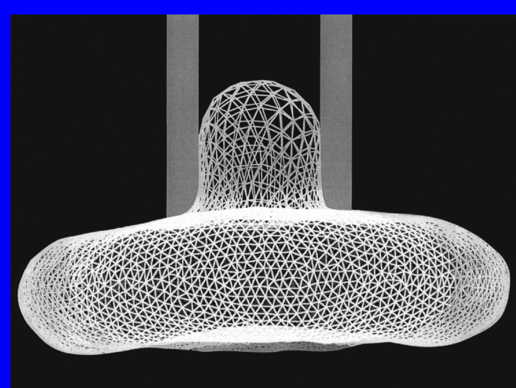
- Part 1: Introductory
  - Building Blocks of Cells
  - Nucleus
  - Cytoskeleton
  - Adhesions

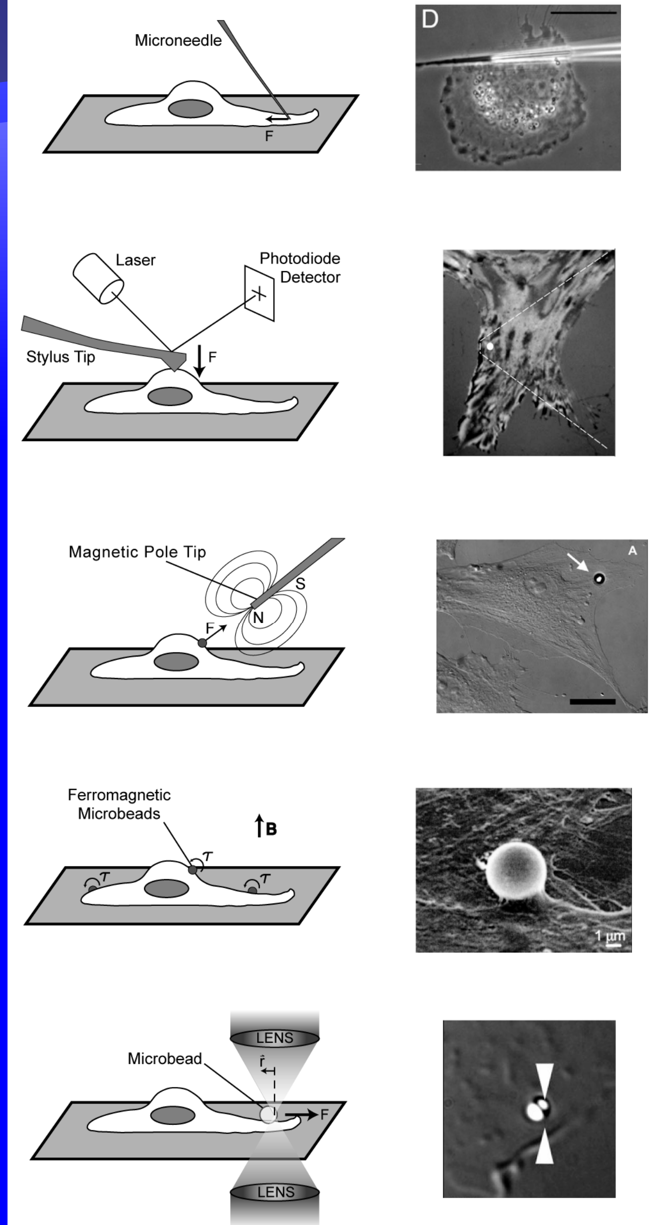




Review of ME599F

- Part 2: Cell Mechanical Analysis
  - Cell Poking
  - Micropipette Aspiration
  - Atomic Force Microscopy
  - Microrheology
  - Magnetic Twisting Cytometry
  - Optical Tweezers



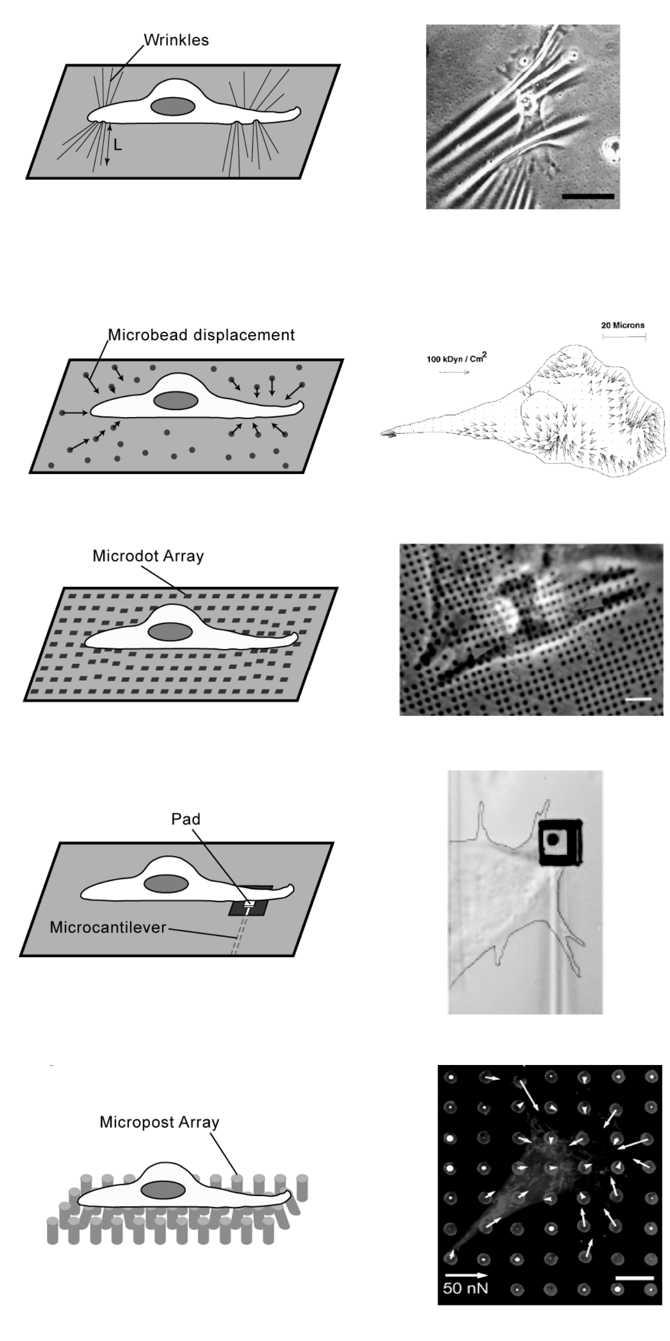


Review of ME599F

- Analysis and Modeling of Cell Mechanics
  - Part 3: Modeling Cell Mechanics
    - Discrete Systems
      - Lumped Parameter Models
      - Tensegrity
      - Foams
      - Flexible Polymer Networks
    - Continuous Systems
      - Simple Lipid Vessels
      - Soft Glassy Materials
    - Computational Models
      - Passive Mechanical Properties
      - Active Bio-Chemo-Mechanical Properties

Review of ME599F

- Part 4: Cellular Forces
  - Silicone Wrinkling Membranes
  - Continuous Substrata
    - Traction Force Microscopy
    - Microdot Arrays
  - MEMS tools
    - Horizontal silicon cantilever
    - Vertical arrayed silicone posts



Review of ME599F

- Analysis and Modeling of Cell Mechanics
  - Part 5: Mechanotransduction
    - Examples
      - Hearing
      - Touch sensitivity
    - Whole Cell Studies
      - Stretch
      - Shear Flow
    - Nanoscale Studies
      - Optical Tweezers
      - AFM
    - Mechanisms

What is Cell Mechanics?

- "The subject of cell mechanics encompasses a wide range of essential cellular processes, ranging from macroscopic events like the maintenance of cell shape, cell motility, adhesion, and deformation to microscopic events such as how cells sense mechanical signals and transduce them into a cascade of biochemical signals ultimately leading to a host of biological responses."

-- Mofrad & Kamm

QUESTIONS?