Session 6

CELL POKING

Class Organization

- Hw3 online. Due Wed 1/30/13

31 years ago…

- U.S. President: Ronald Regan
- Lebanon war begins
- Graceland opens
- USA Today is first published
- AT&T "monopoly" is broken apart
- Compact discs hit the market
- First artificial heart implanted in Barney Clark

31 years ago…

1 January 1982, Volume 215, Number 4528

SCIENCE

Luck, Merit, and Peer Review

Every year the National Science Foundation spends a billion dollars, mostly on the support of research. A recent report commissioned by the foundation* suggests that chance enters significantly into decisions of the peer review system by which NSF evaluates funding requests for scientific research. The report indicates that about 25 percent of NSF decisions would be reversed by a different panel.

"Capital punishment," or loss of grant support, is cruel, but no longer unusual, in academia. The notion that chance enters into the decision-making process adds a special twist, and this study has raised calls from many quarters for elimination of the peer review system—a reaction not at all justified by the findings. Distribution of research funds in block grants to states or by random lottery, both of which have been suggested, would foster mediocre research.

We have become chary. We insist on certainty whether or not it is practical. We want zero levels for pollution, accountability of school teachers for what our children learn, and guarantees that the products we buy will not break, wear out, or cause injury. If disappointed, we sue for damages.

But honest scientific research is a gamble. The peer review system is probably the best method the NSF has for placing its chips. Every time a bet is placed, something is risked. We might reduce the uncertainty considerably by doubling the number of readers for each proposal. Would this be worthwhile?

In the peer review system, a proposal is evaluated independently by "peers" chosen from a pool of reviewers qualified in the area of the proposal. In most areas, only proposals rated "excellent" or "very good"

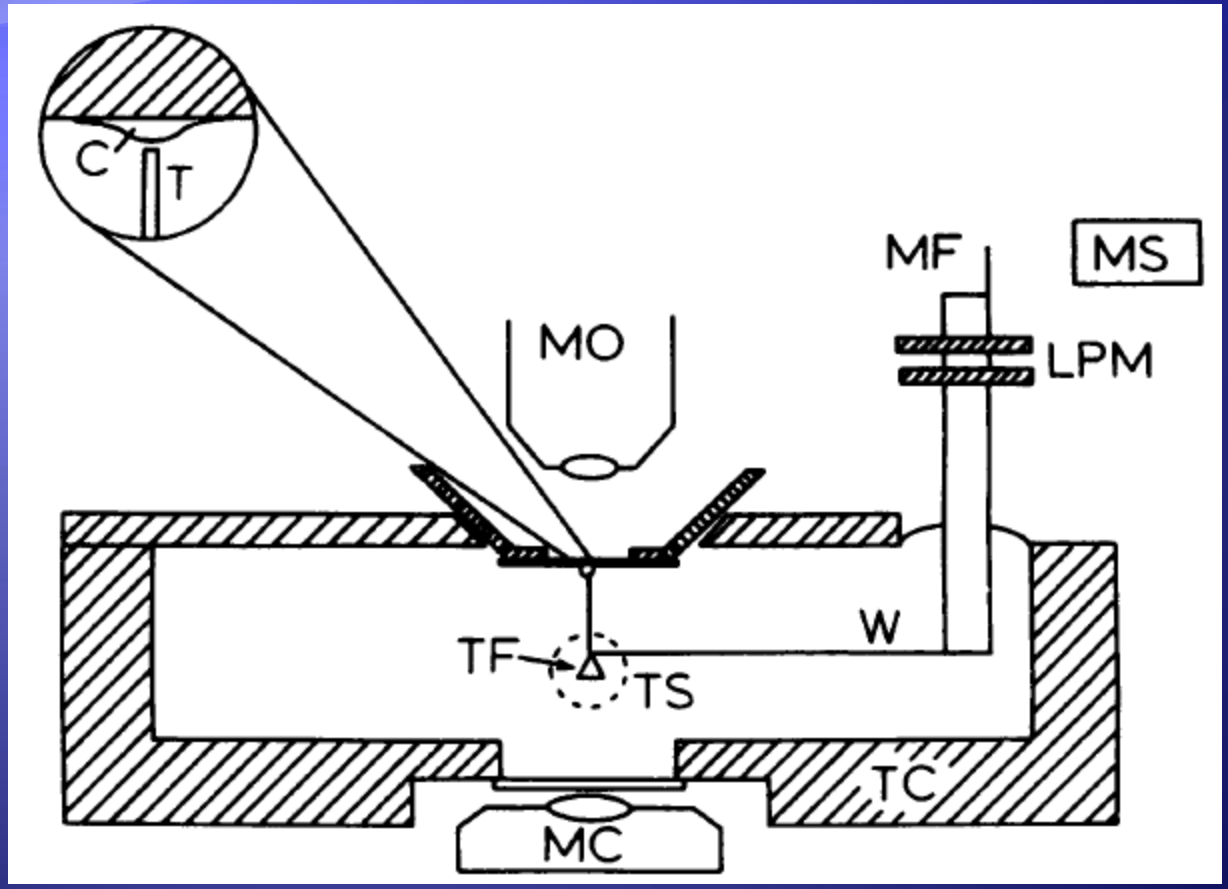
The Hypothesis…

- Since cells function mechanically by changing shape, forces that control shape (e.g. actin polymerization) must be relate to forces that drive mechanical activities

The Impact…

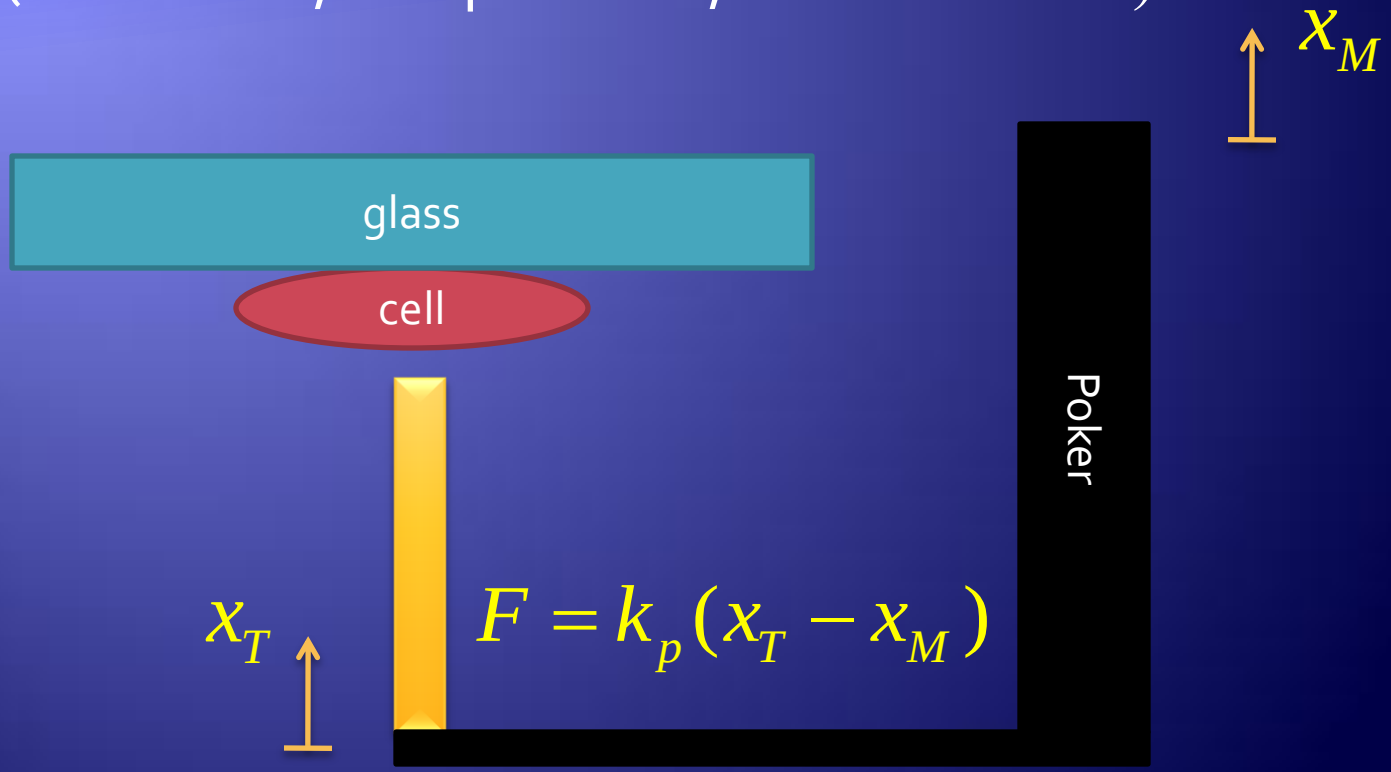
- Direct measurement of cellular mechanical properties
- Microfilaments (actin) determine cellular mechanical properties

The Apparatus…

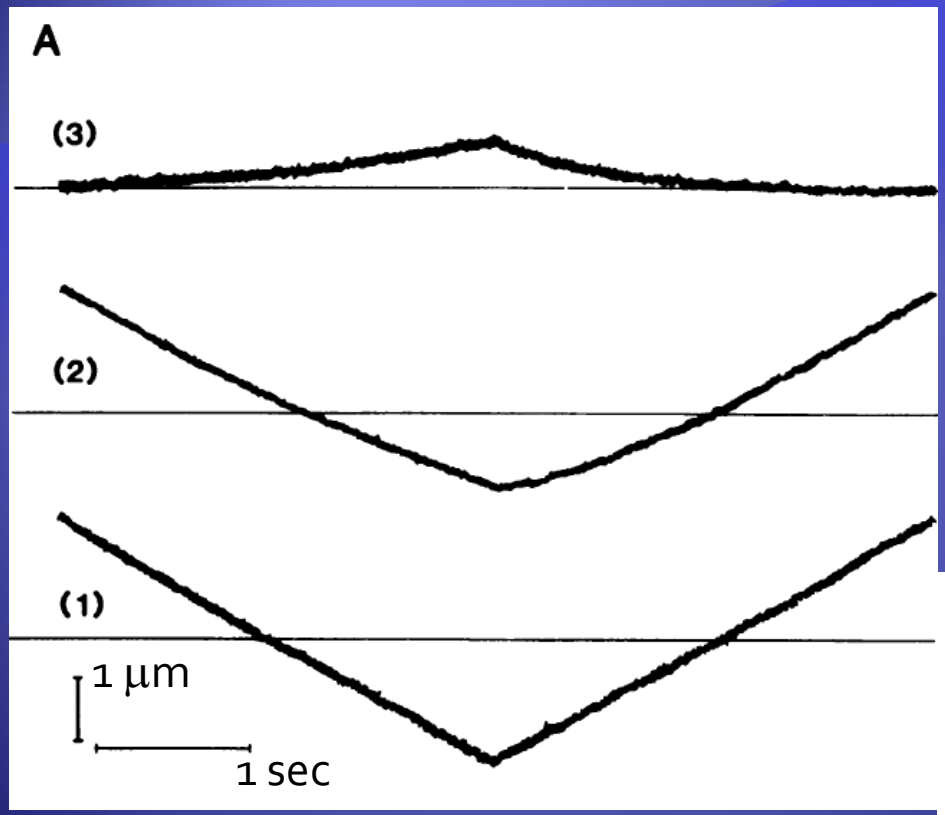


The Measurement

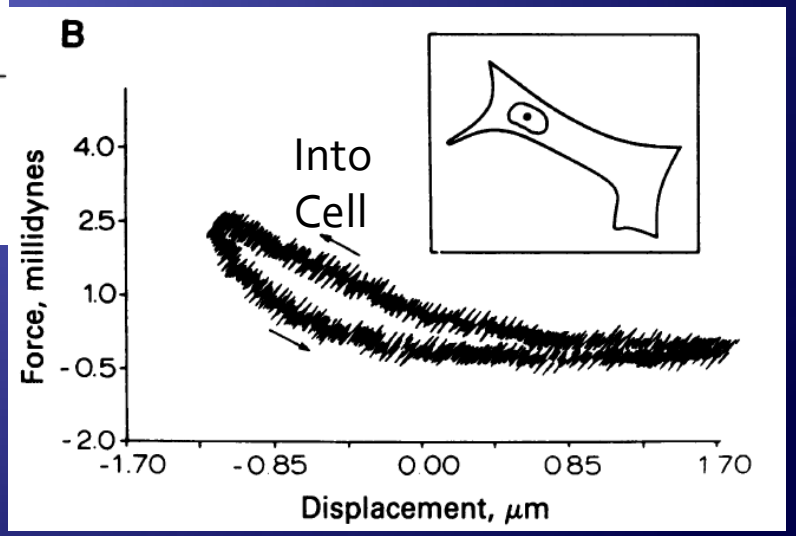
- Two springs in series
  - Poker: k_p(modulus, dimensions)
  - Cell : k_c(strain rate, temperature, CSK structure)



The Test

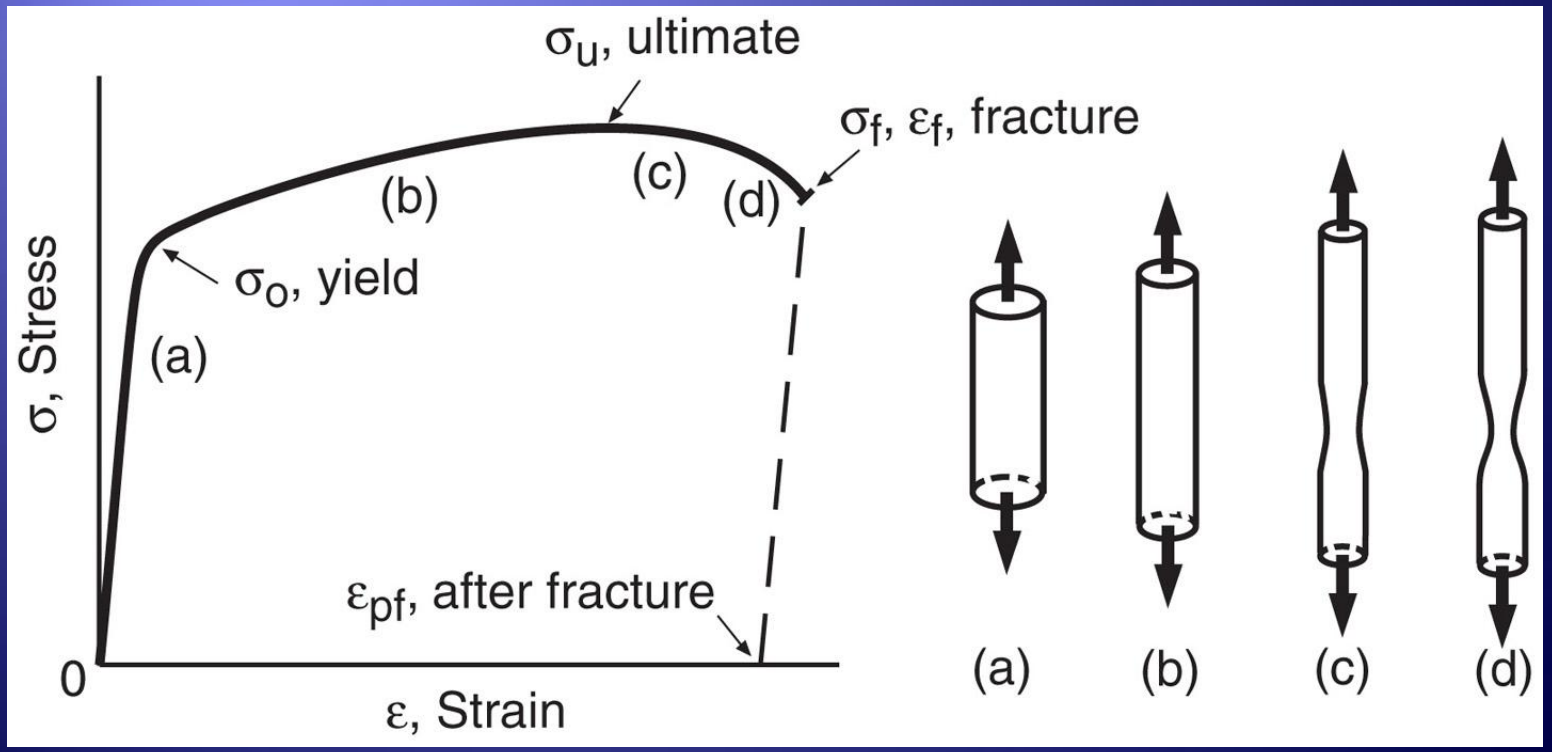


- k = 3.8 millidynes/µm
  - 1 dyne = 1 x 10^{-5} N
  - 1 millidyne = 10 nN
  - → 38 nN/µm



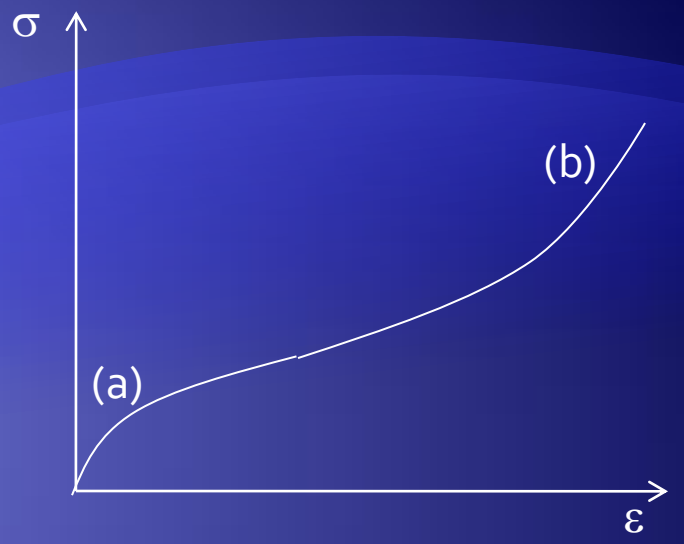
Elasticity, Plasticity

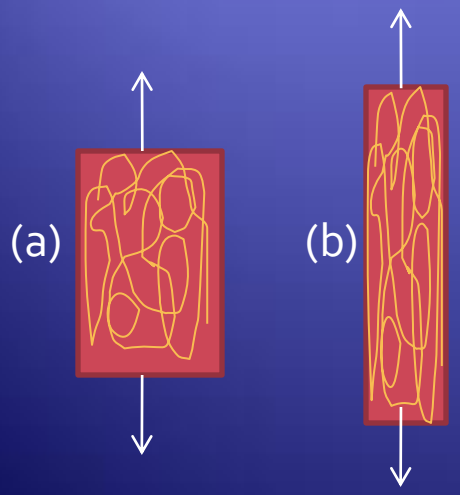
- Metals deform elastically (recoverable) but after yielding they deform elastically but with permanent strain (unrecoverable)

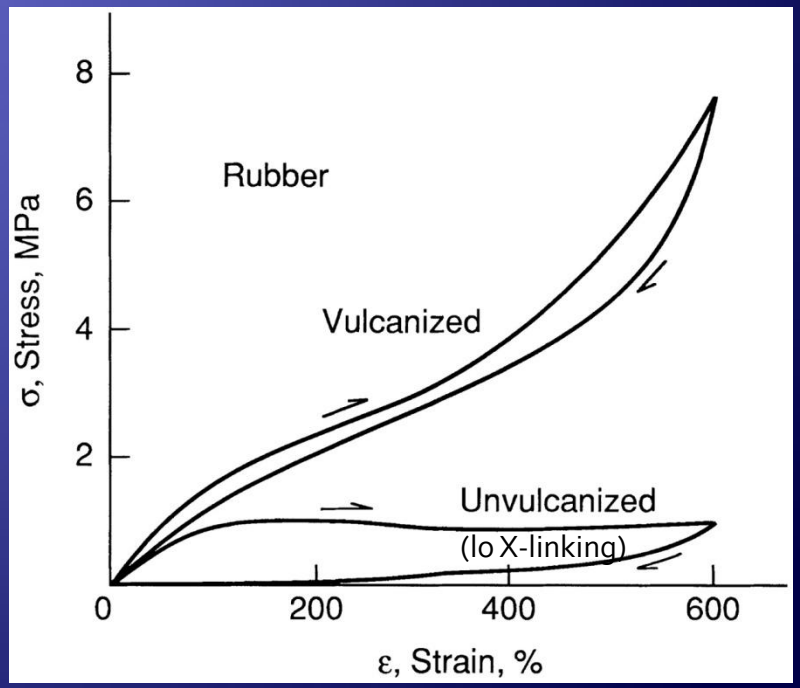


Elastomers

- Rubber has S-curve
- Mechanics depends on polymer chains
- Hysteresis is path-dependence
- Vulcanizing promotes cross-linking between polymer chains

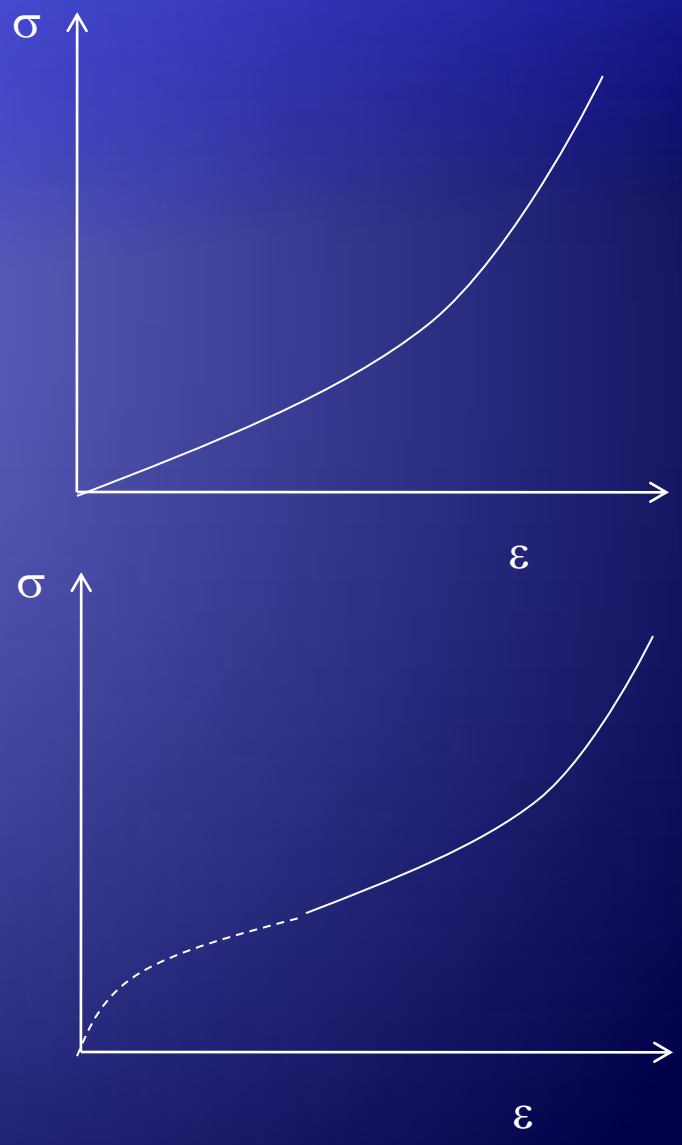






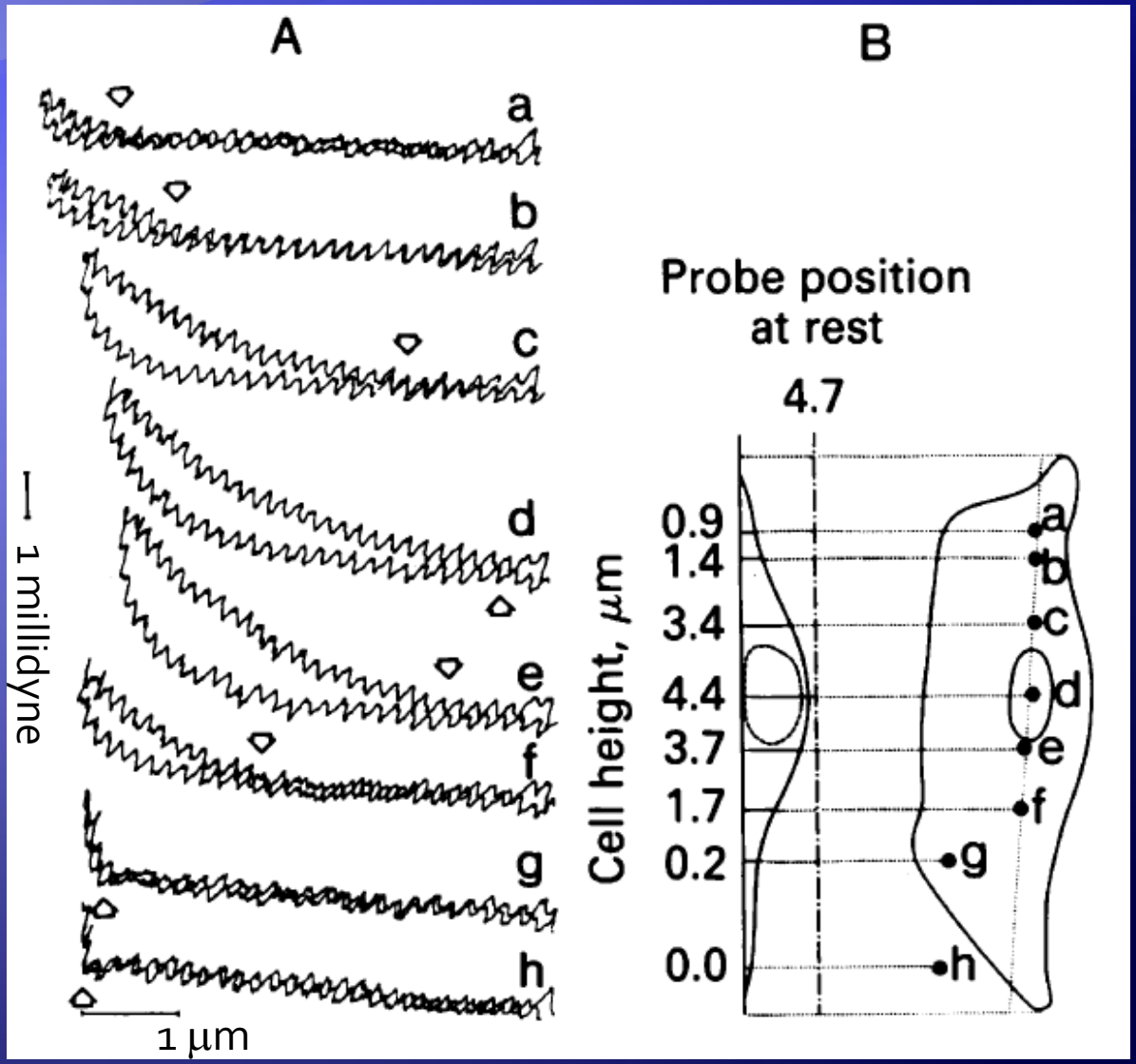
Biomaterials

- J-curve
- Behavior due to increased alignment of fibers
- Think of stretching your earlobes
- J-curve is an S-curve with pre-stress



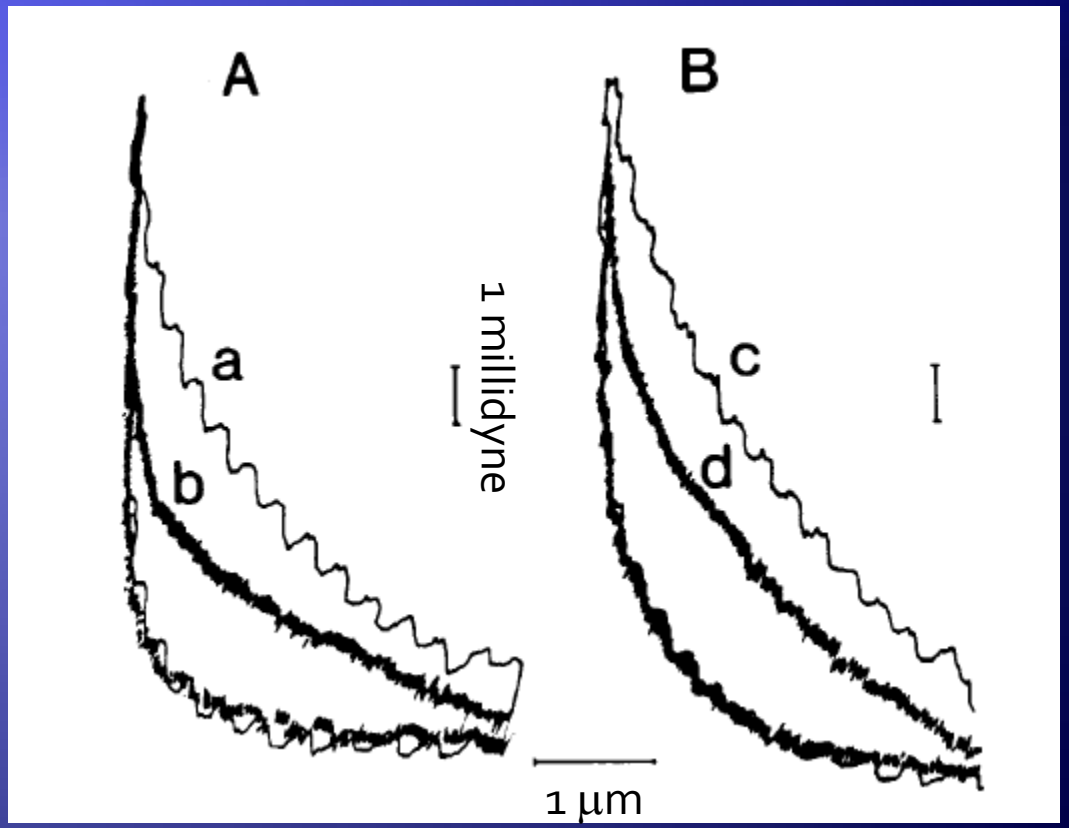
Spatial Probing

- Arrows indicate point of contact
- Low hysteresis in thinner regions
- Initial k_{cell} =0.6 millidynes/μm
- Increased k_{cell} with depth of penetration



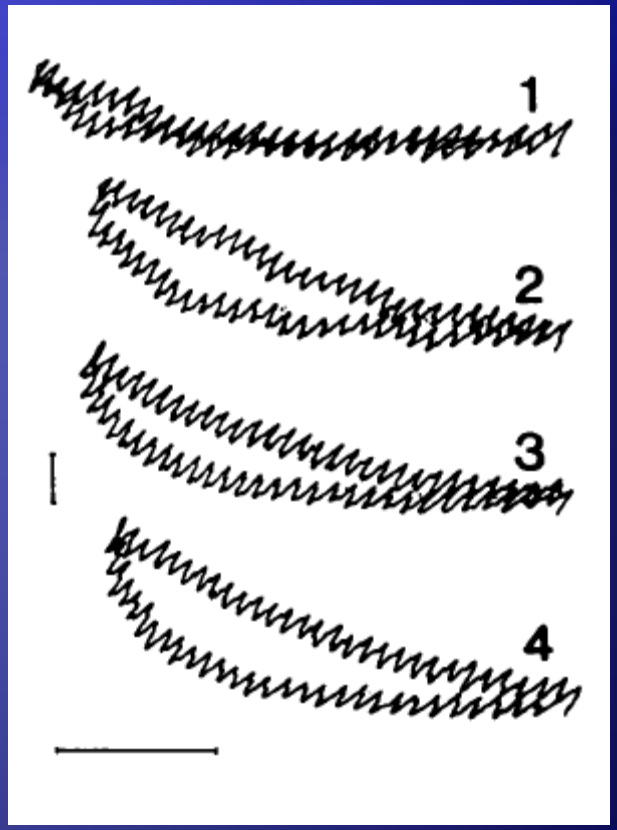
Strain Rates

- 21 vs 2.1 μm/s
- Near nuclear (A)
  - Hi strain rate, hi stiffness
  - Lo strain rate, lo stiffness
- On nucleus (B)
  - Hi or Lo strain rate have same stiffness



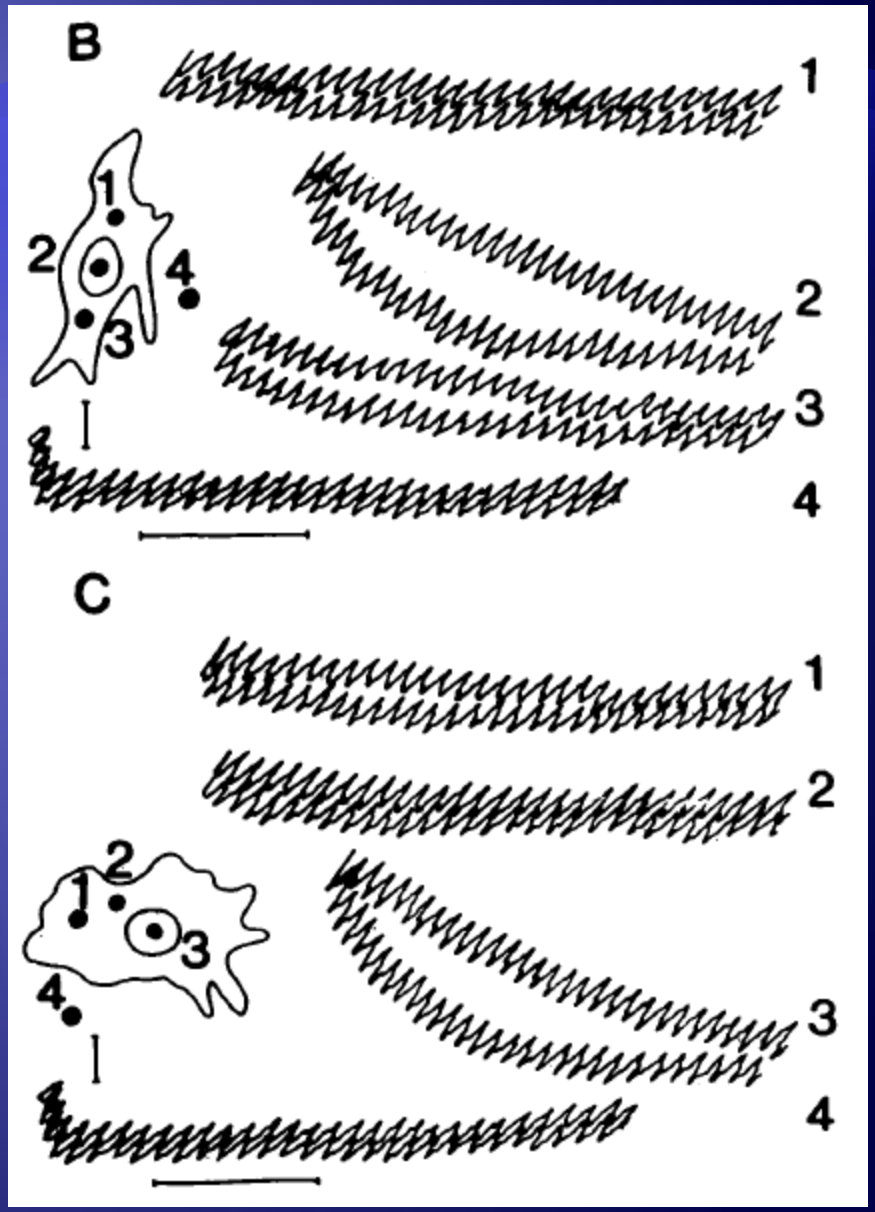
Temperature

- Previous tests at 22° C
- Lower hysteresis at 37° C
- Lower stiffness at 37° C
- Thermal expansion problem in set-up?



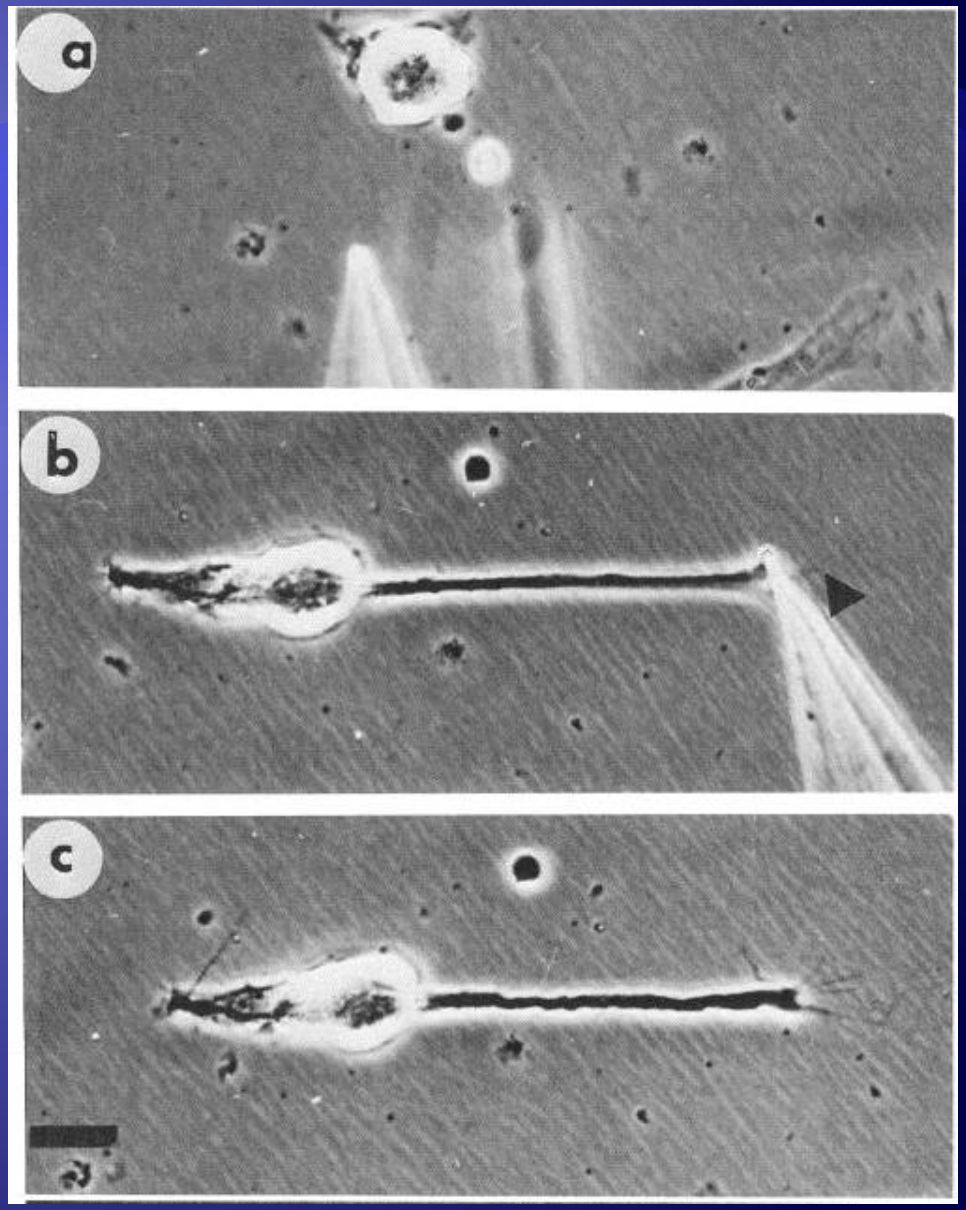
Cytochalasin B

- Two cells incubated with 10 μg/ml for 1 hr
- Cell 1 (tested 8-14 min after wash-off)
- Cell 2 (tested 23-32 min after wash-off)
- No effect to nuclei
- Cytoskeleton is softer



Neuron Poking

- Tension from glass microneedle can form neurite extension from chick sensory neuron cells



Zheng, …, Heidemann, J Neuroscience, 1991, 11(4):1117

QUESTIONS?