MEMS based sensors for cellular studies

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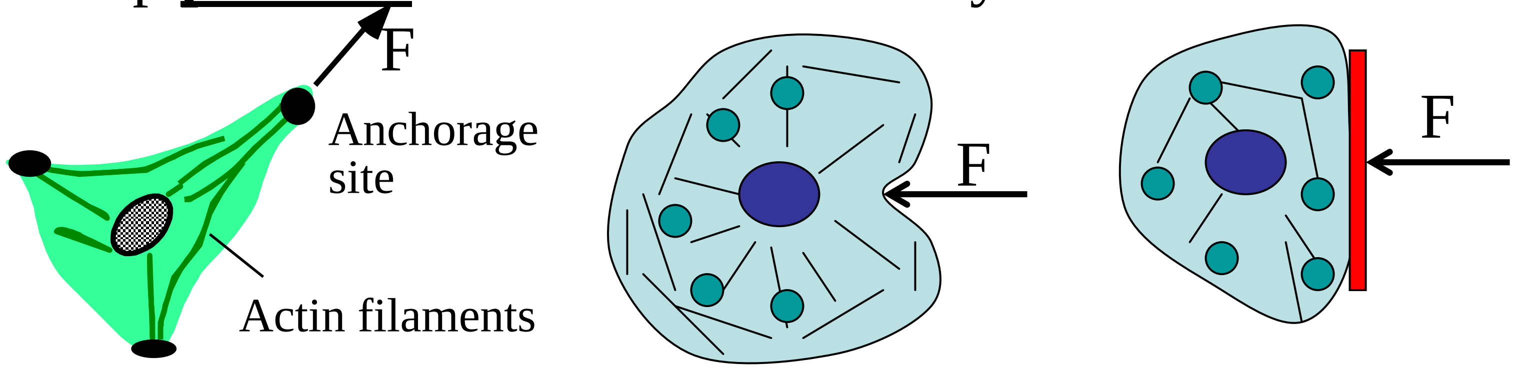
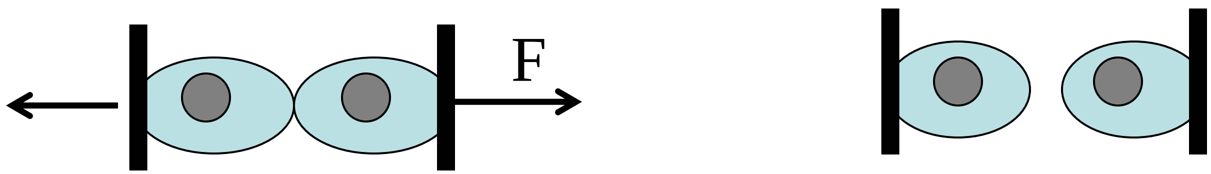
Part of GEM4 Summer School lectures on
instruments for cell mechanics studies (Aug 10, 2006, MIT)

Objective

Develop **portable** micro sensors to study:



• Cell mechanical response

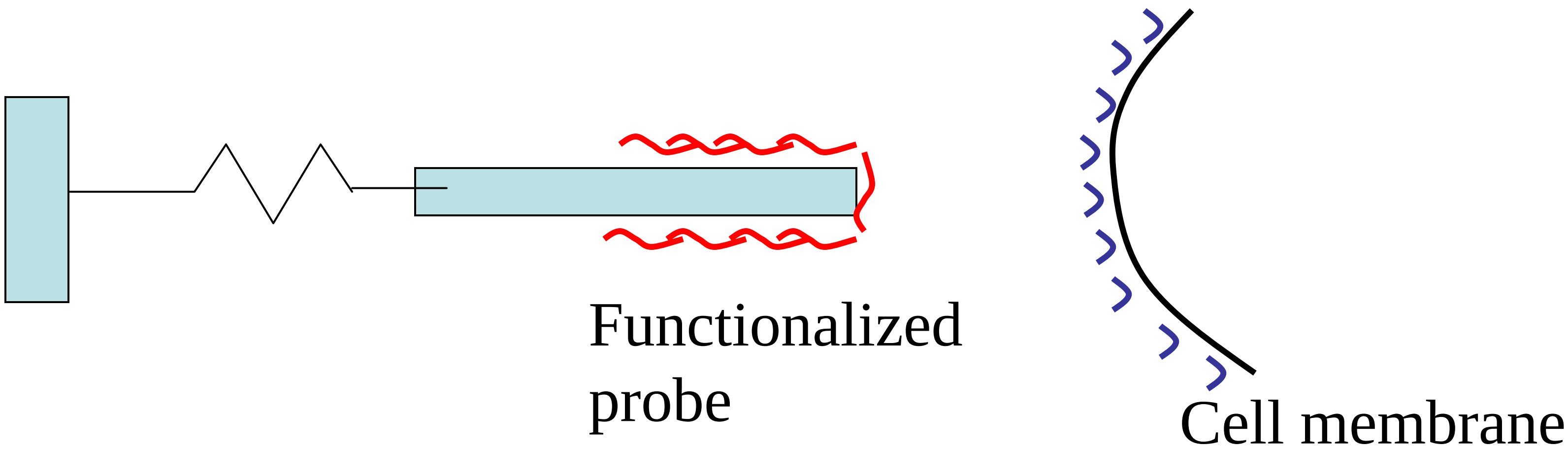


• Cell adhesion

in different biochemical environments
to explore mechanotransduction and disease detection

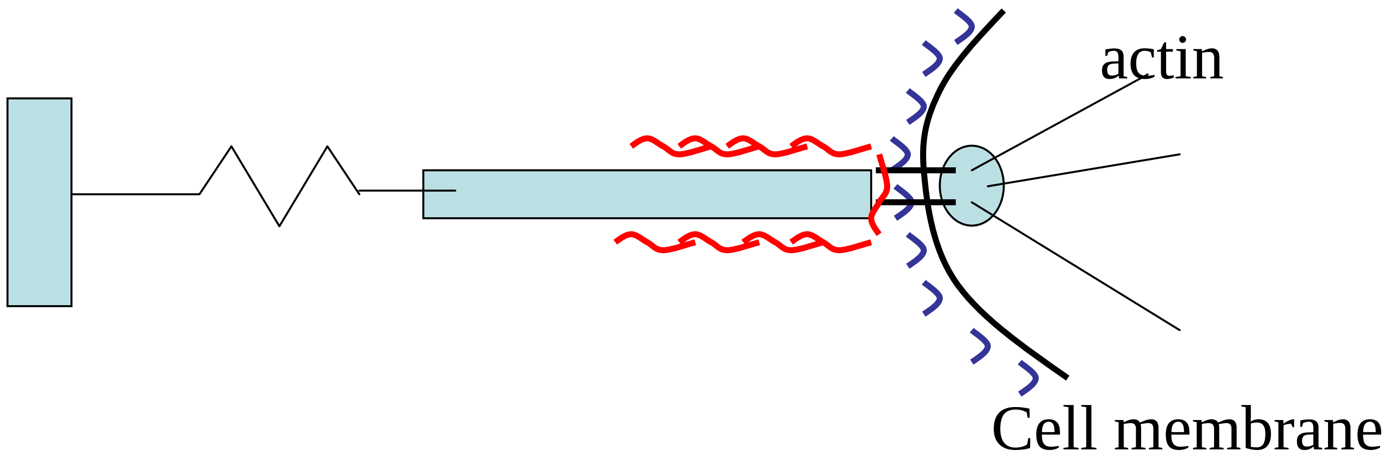
Basic idea

A micro spring is used to measure cell force



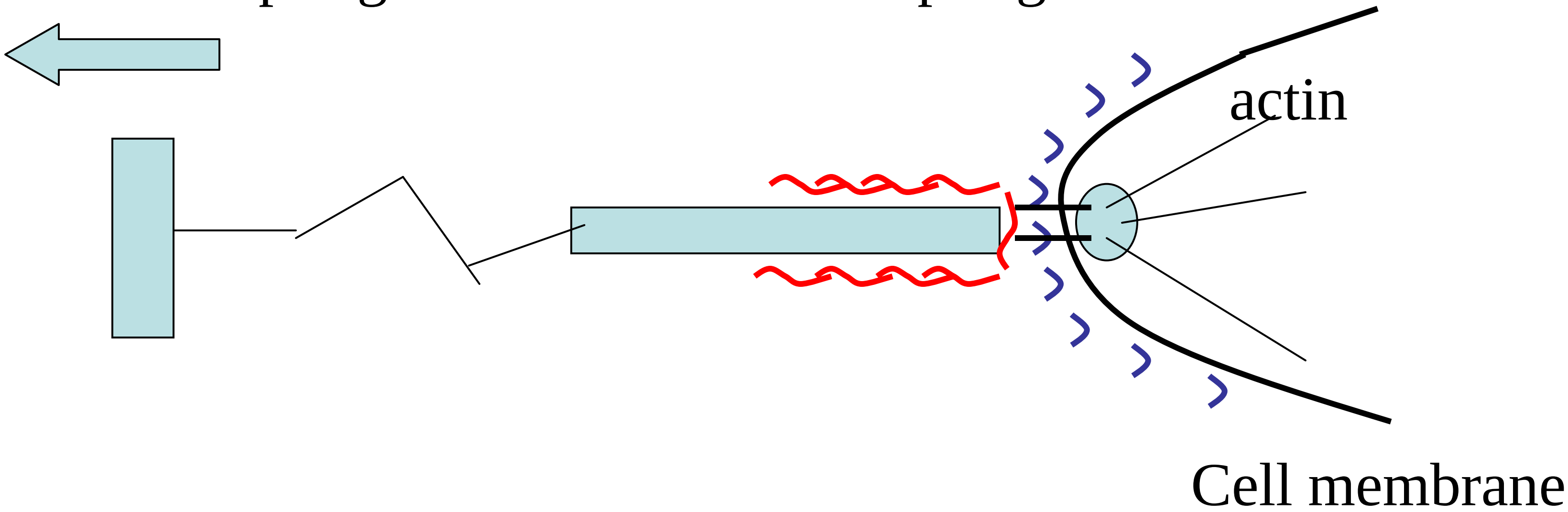
Basic idea

Functionalized probe contacts a cell and forms adhesion site



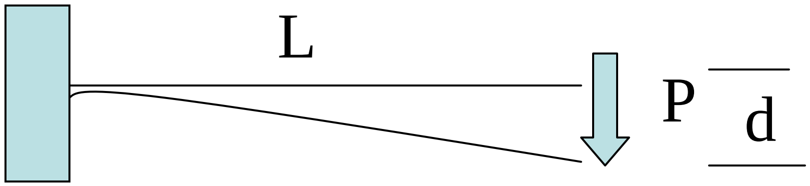
Basic idea

Probe is moved away from the cell. The cell applies a force on the spring. The force is measured from the spring deformation and its spring constant.



The cell may also be compressed or indented.

Cantilever as a mechanical spring



K (spring constant) = $3EI/L^3$

$P = Kd$

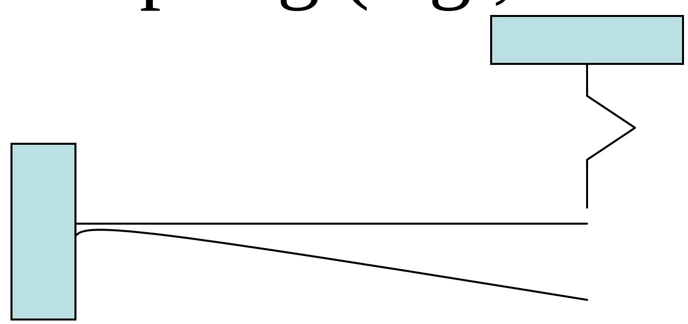
I=moment of inertia = width x depth^3/12

Typical K ~ 10 nN/μm

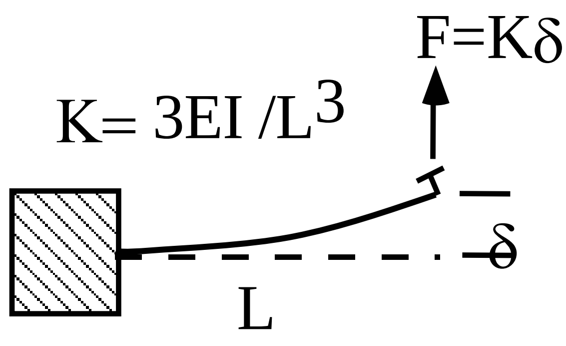
Calibration:

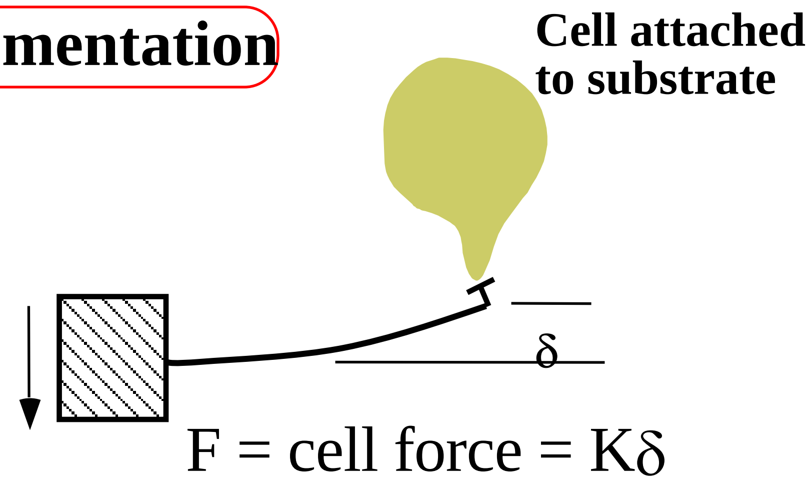
1) Resonant frequency, geometry, elastic property

2) Comparing with another spring (e.g., AFM)



Simple implementation

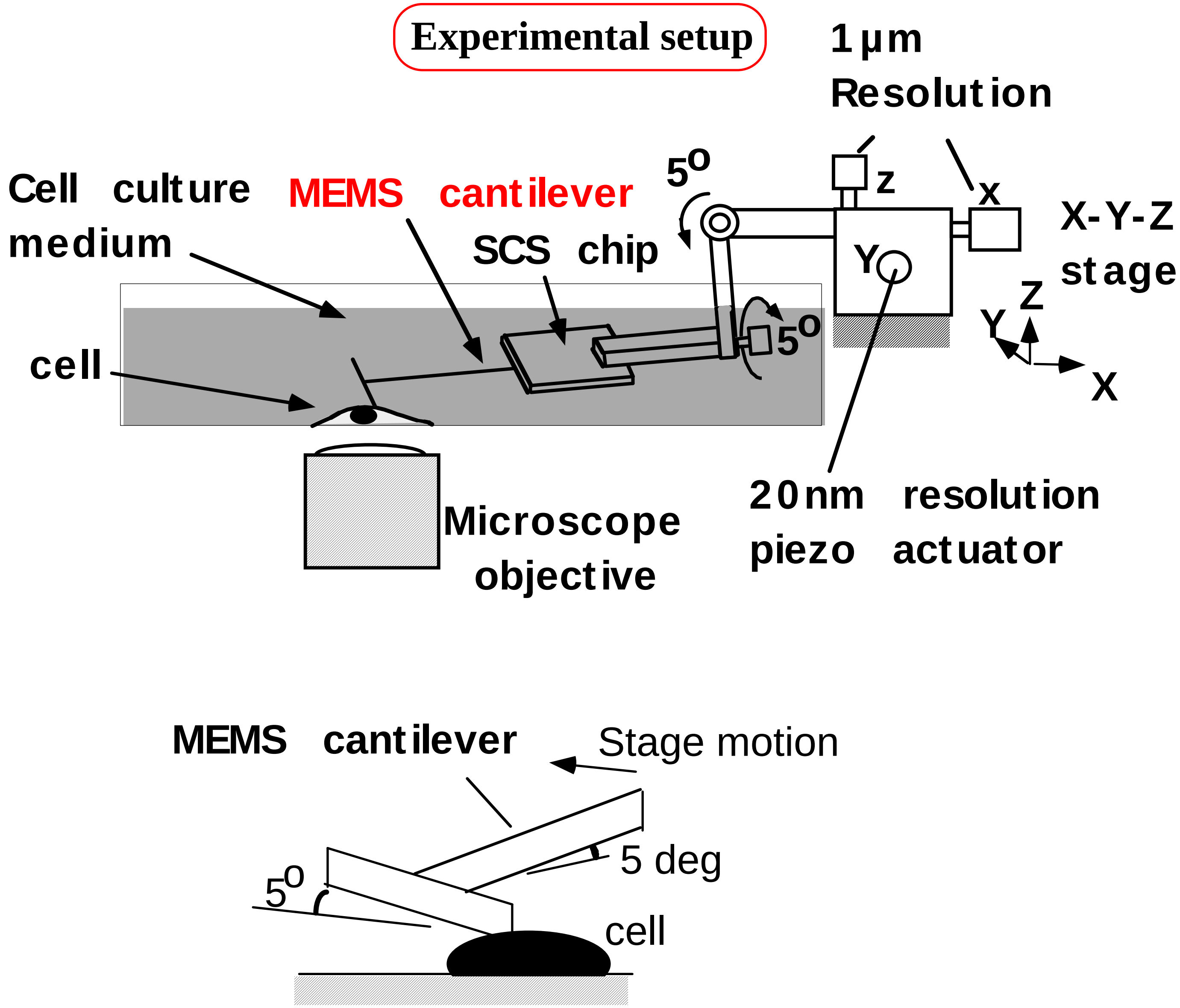




- Force sensor (such as a cantilever) is coated by fibronectin
- It is calibrated to determine spring constant, K
- The sensor tip is brought in contact with the cell - focal adhesion sites form
- It is moved away from the cell. The cell force is measured from the deformation δ

Advantages: - Force sensor independently calibrated
- Force is applied at an anchorage site
- In-situ observation

Experimental setup

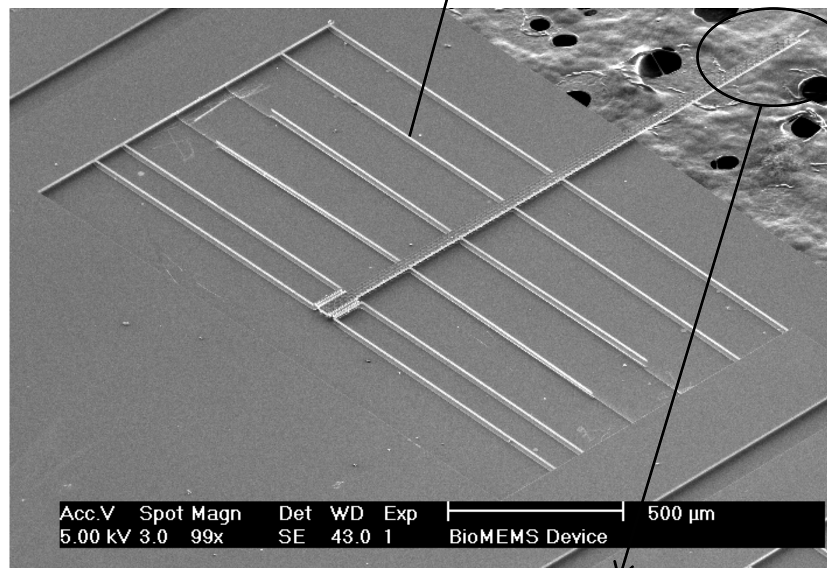


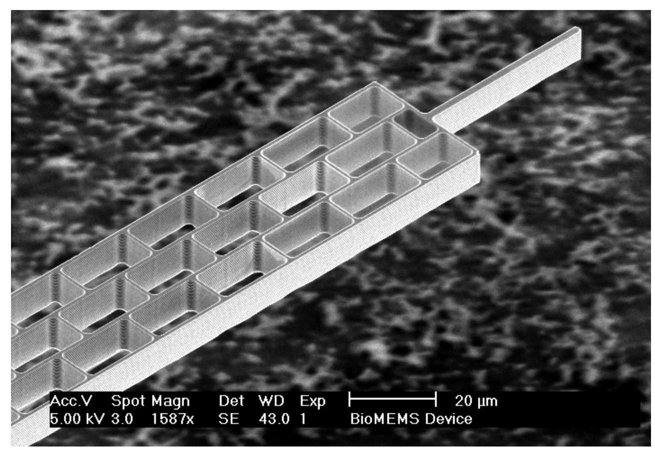
MEMS force sensor: beams anchored at both ends

Example

Figure removed due to copyright restrictions.

Flexural springs (1μm wide)





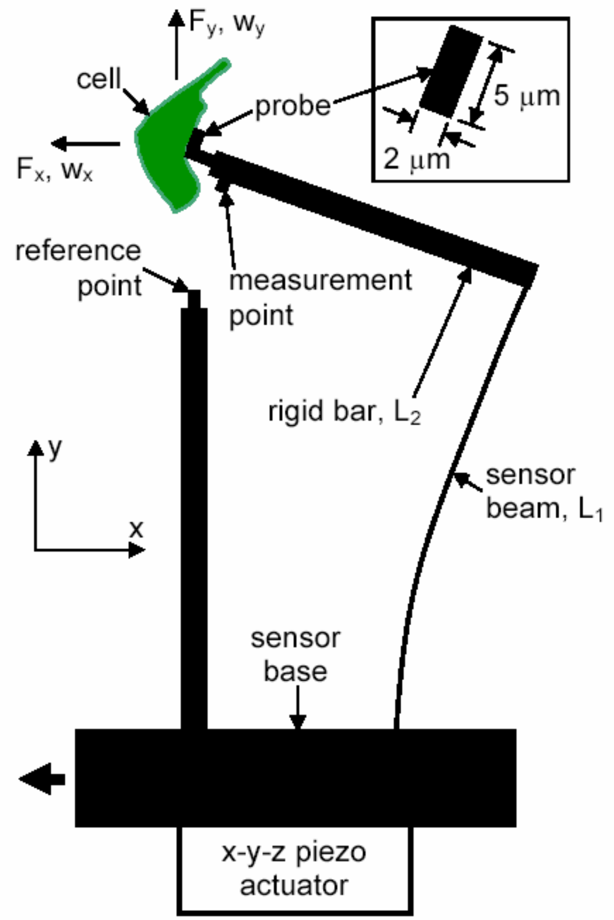
Probe

$K = 3.4$ nN/μm

Yang and Saif.
Review of Scientific Instruments 76, 044301 (2005).

Example

2D force sensor



Example

Endothelial cells in a culture dish with MEMS cantilever

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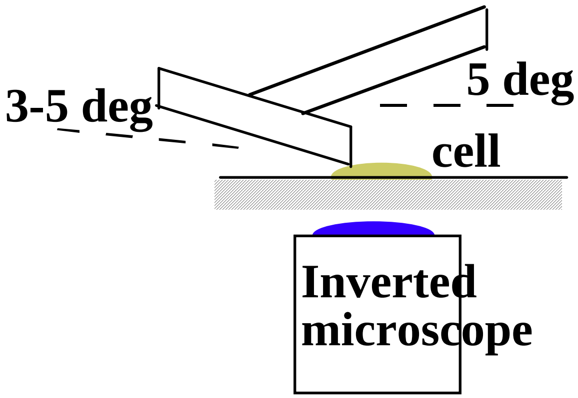
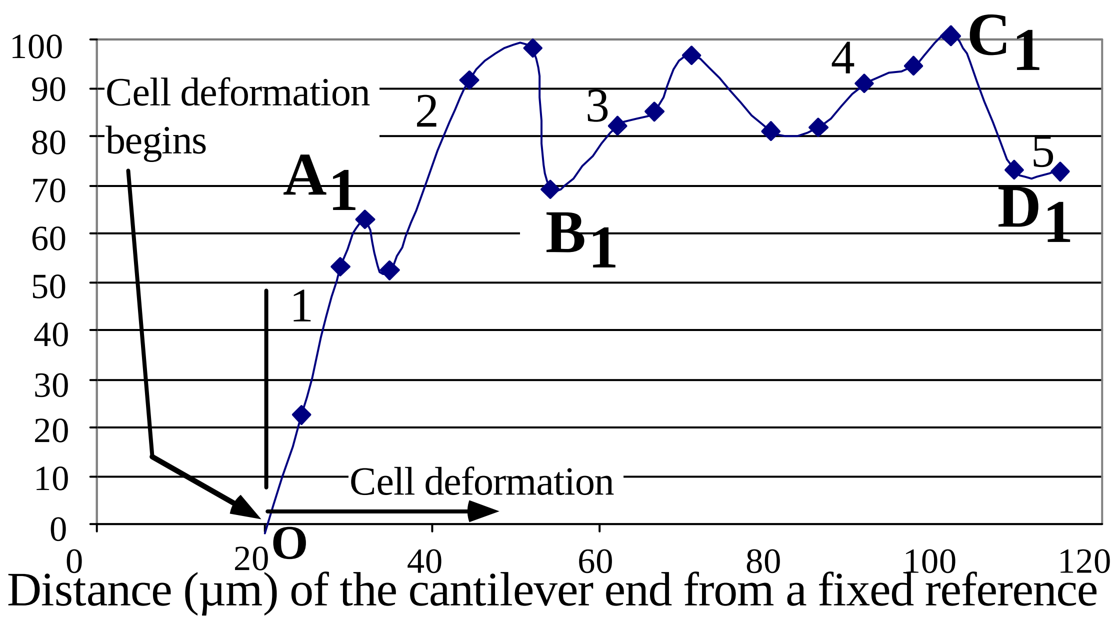


Schematic of the MEMS cantilever

Force response of an endothelial cell



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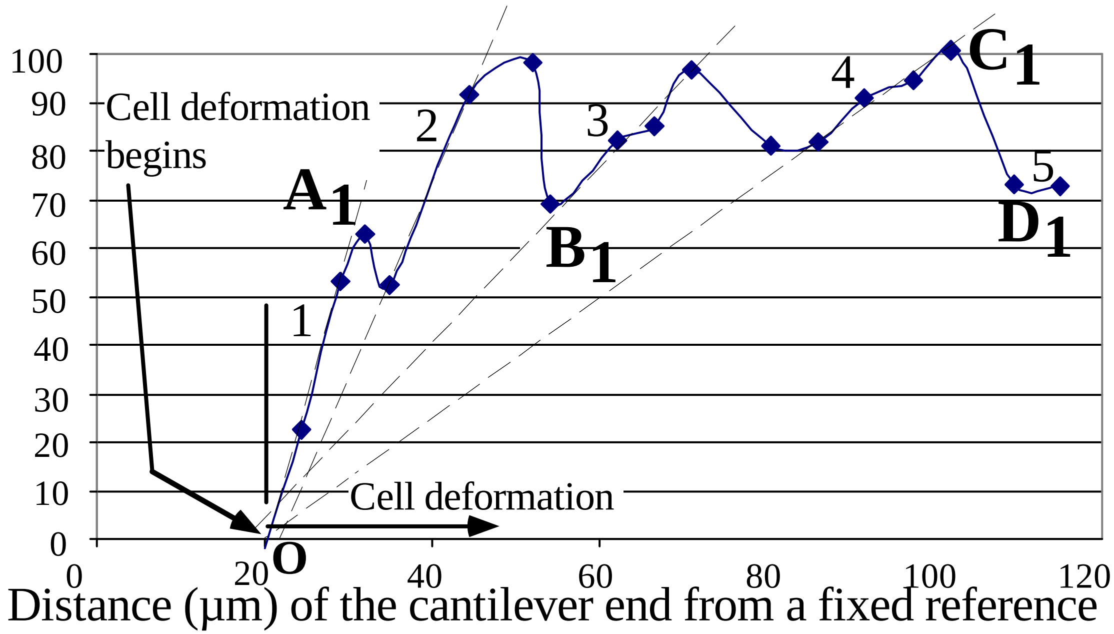
Force response of an endothelial cell



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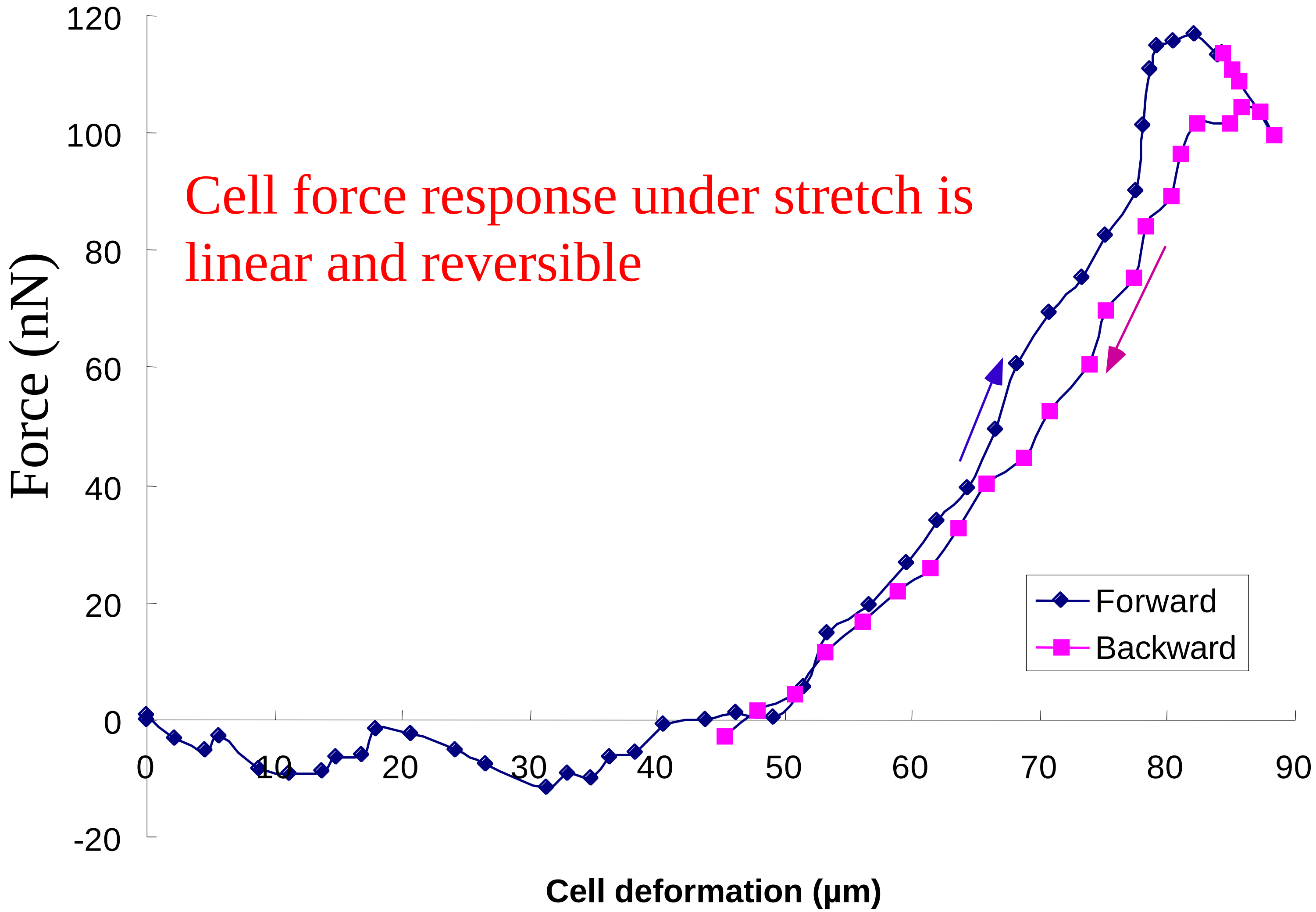
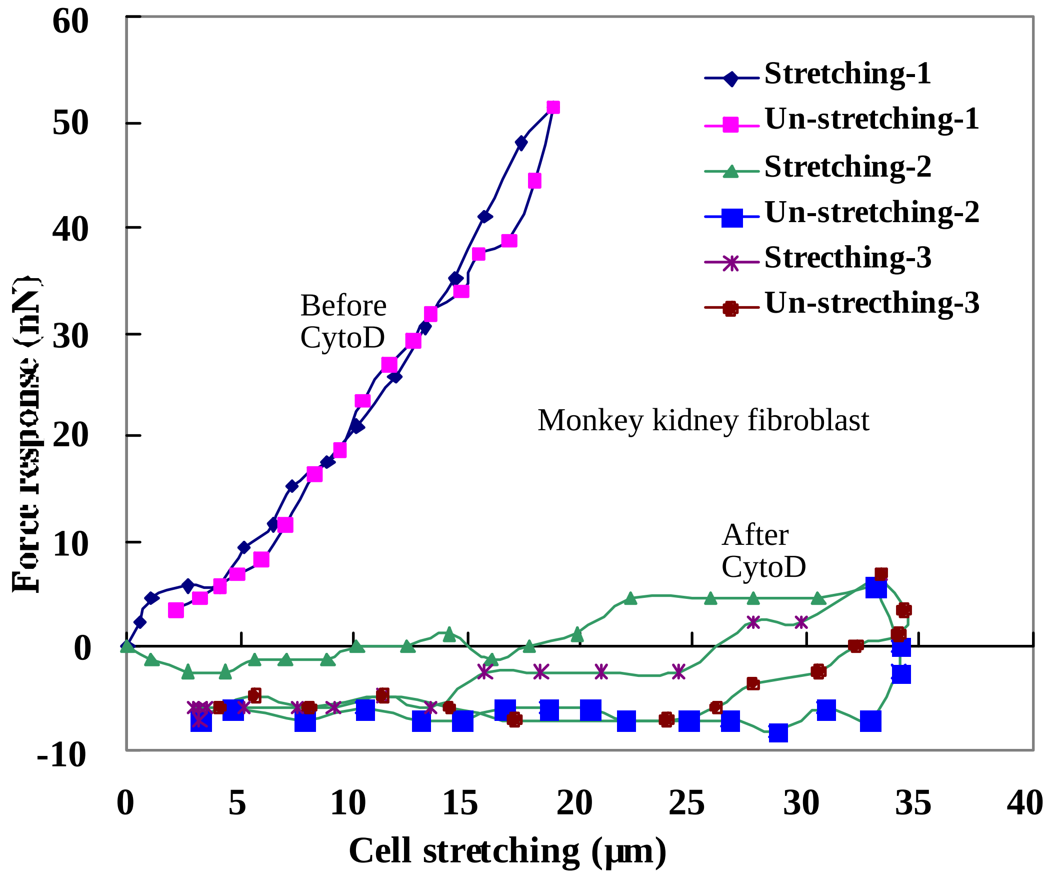
Force response of a monkey kidney fibroblast cell



Reference: Yang and Saif. Experimental Cell Research 305 (2005) 42– 50.

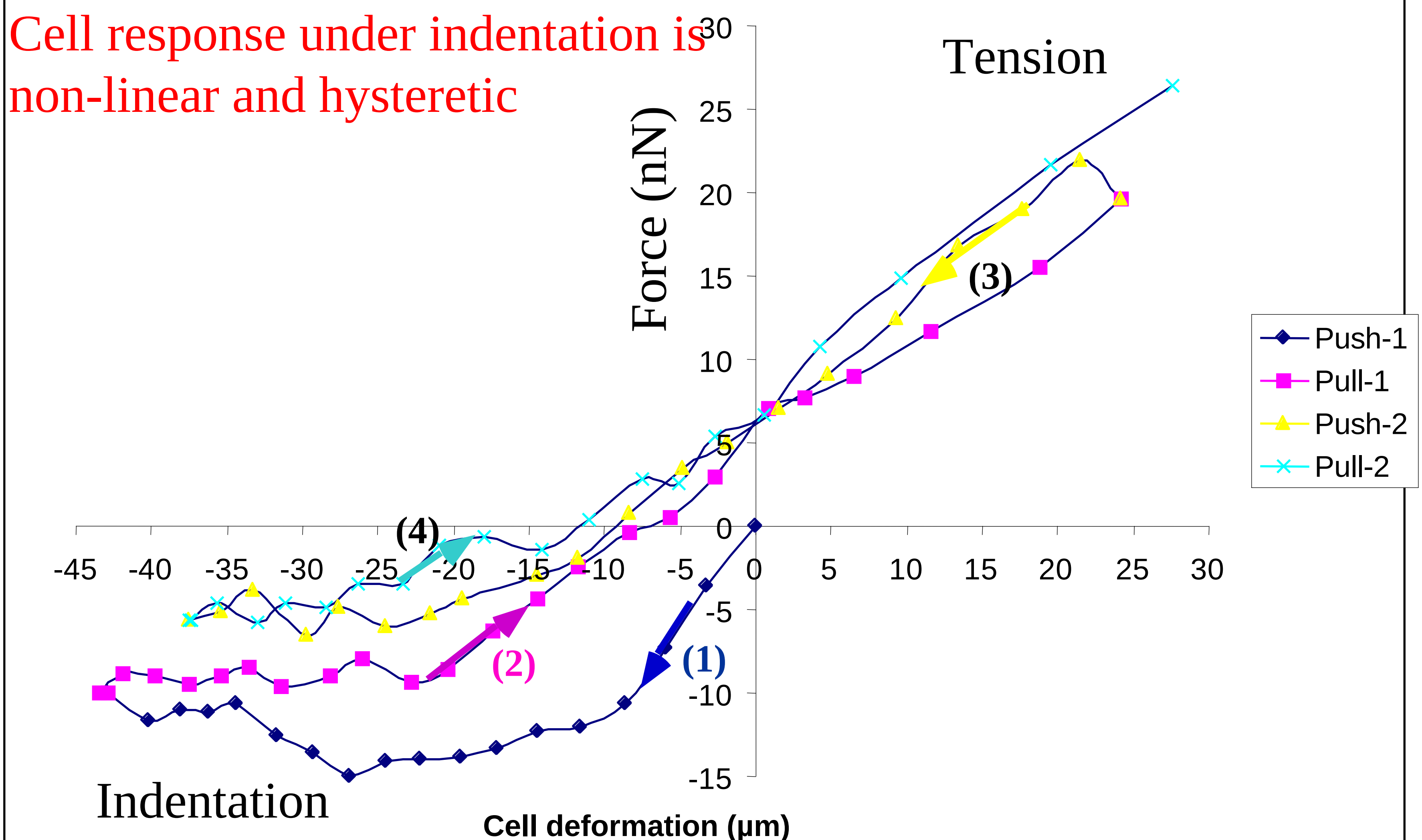
Cyto-D treatment disrupts force bearing capacity



Cyto-D disrupts actin network

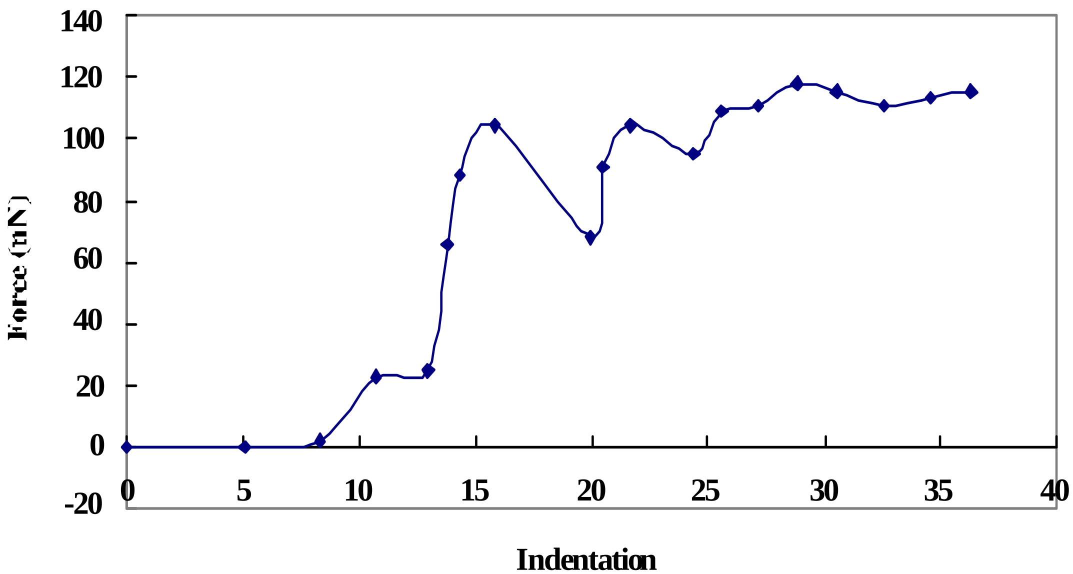
Reference: Yang and Saif. Experimental Cell Research 305 (2005) 42– 50.

Force response of a monkey kidney fibroblast cell



Mechanism of non-linearity and irreversibility under indentation

Image removed due to copyright restrictions. Photograph of GFP actin protein.



Actin agglomerates irreversibly under indentation

Images removed due to copyright restrictions.
Images of GFP actin undergoing indentation.

Yang and Saif
Actabiomaterialia 2006 (in press)

More evidence of actin agglomeration

Images removed due to copyright restrictions.
Actin in monkey kidney fibroblast is subjected to indentation.

Monkey kidney fibroblast subjected to mechanical indentation (injury simulation). Here actin stress fibers are highlighted by green florescent protein (GFP). In response to indentation, the cell signals local actin agglomeration at discrete locations. Such actin agglomeration is also observed in various physiological conditions such as during ischemic attack in kidney cells. This is the first evidence of actin agglomeration due to mechanical stimulus (Shengyuan and Saif, Actabiomaterialia 2006, in press).

Actin agglomeration in physiological condition: ischemic attack

Image removed due to copyright restrictions.
Figure 5c in Ashworth, Sharon L., et al. "ADF/cofilin Mediates Actin Cytoskeletal Alterations in LLC-PK Cells During ATP Depletion."
American Journal of Physiology - Renal Physiology 284 (2003): F852-F862.

Porcine kidney cells

Ashworth et al. Am J. Physiol Renal Physiol 284: F852, 2003.

Why MEMS bio sensors:

1. Force range: 1-100 nN (natural progression from optical tweezer, magnetic beads, AFM)

1. Flexibility of design (cell contact region may be designed in a variety of fashions)

3. Large cell deformation range (sub μm-10s of μm)