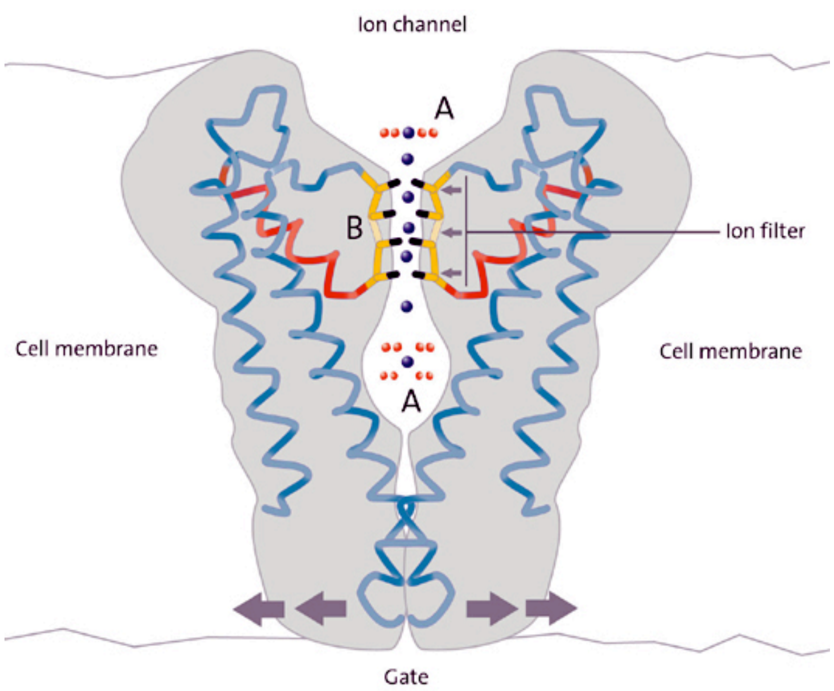
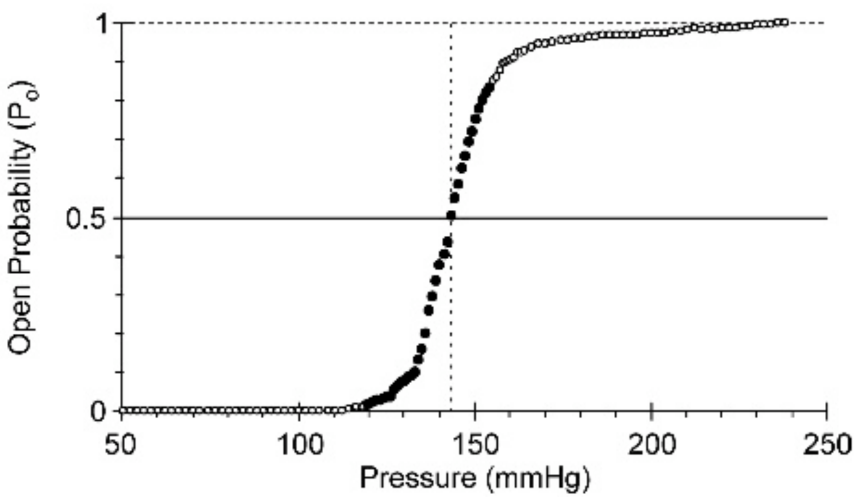
MEMS for Mechanotransduction

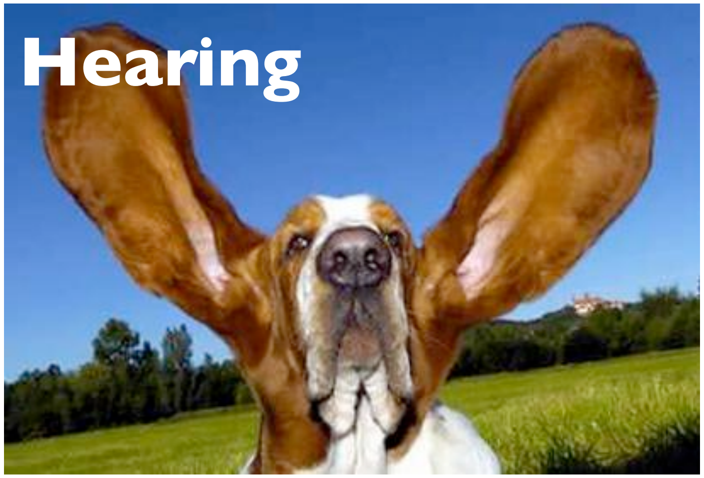
Joey Doll

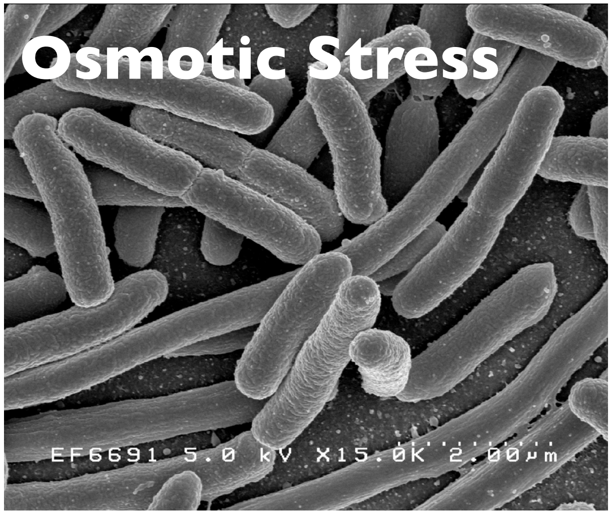
Mechanically Gated Ion Channels





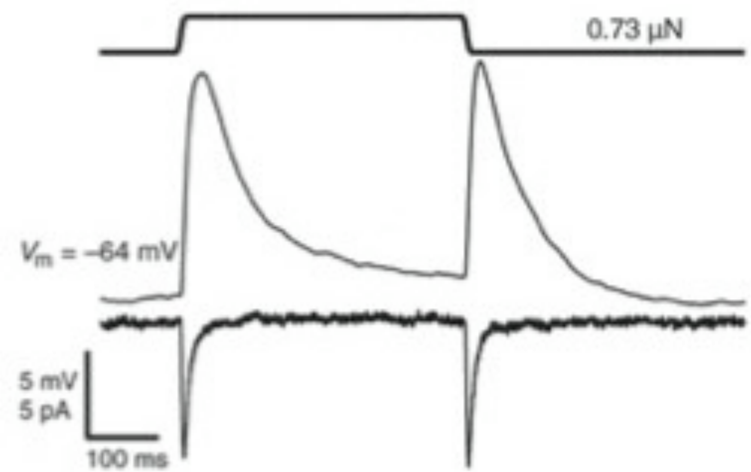
Their Importance to Life





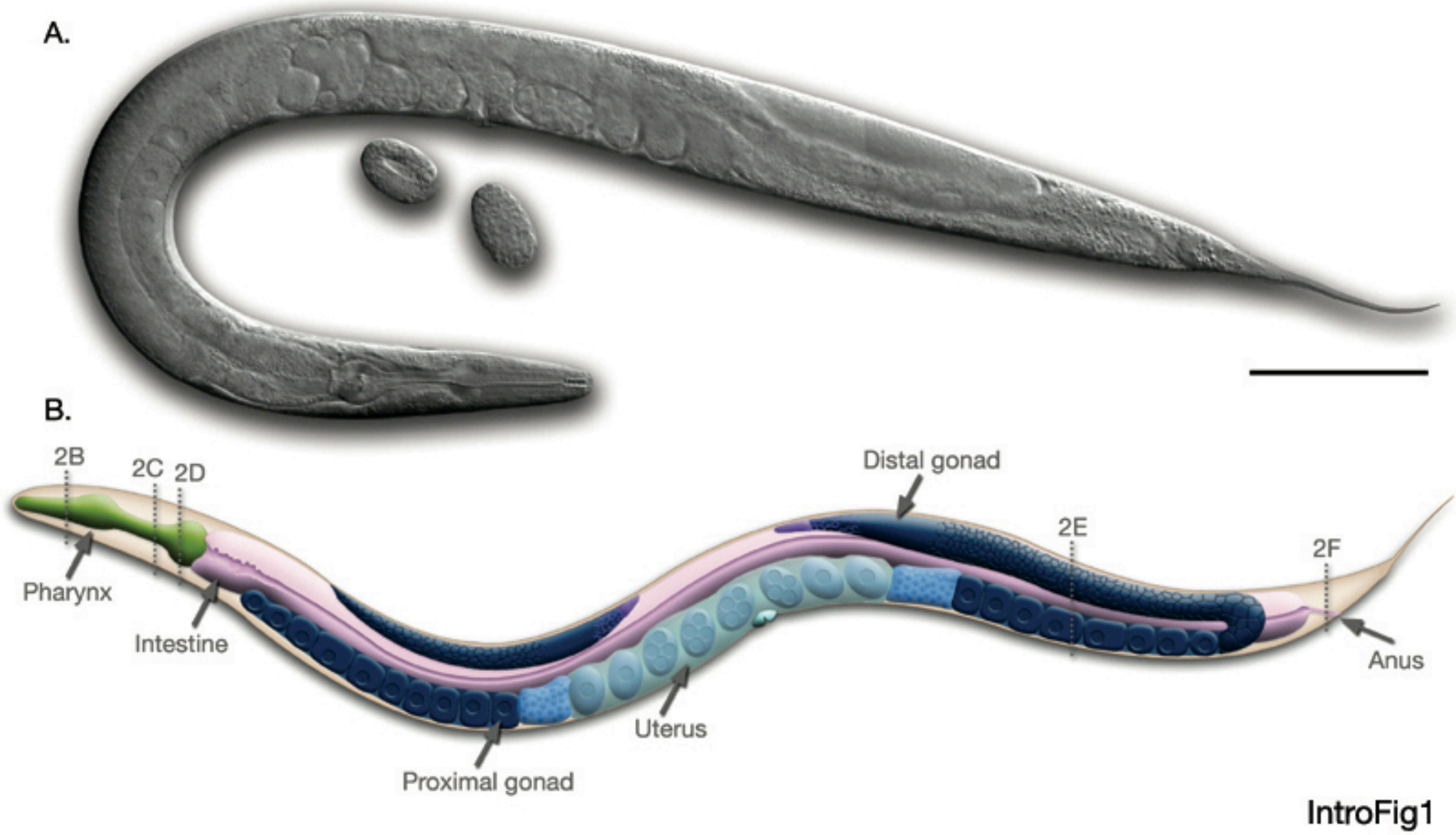
Work to Date

- Touch receptor neurons (TRNs) are mechanosensitive
- Known
  - Ion channel identity
- Unknown
  - Adaptation mechanism
  - Gating mechanism
  - Opening/closing kinetics
  - Only *in vivo*



O'Hagan, Chalfie and Goodman, The MEC-4 DEG/ENaC channel of *Caenorhabditis elegans* touch receptor neurons transduces mechanical signals, Nature (2004)

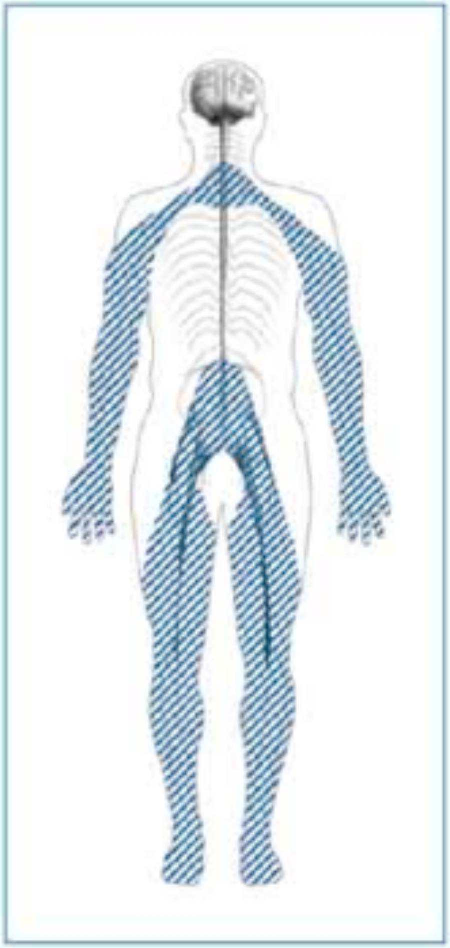
C. elegans



A.
B.
2B
2C
2D
Distal gonad
2E
2F
Pharynx
Intestine
Uterus
Proximal gonad
Anus
IntroFig1

Why is this Important?

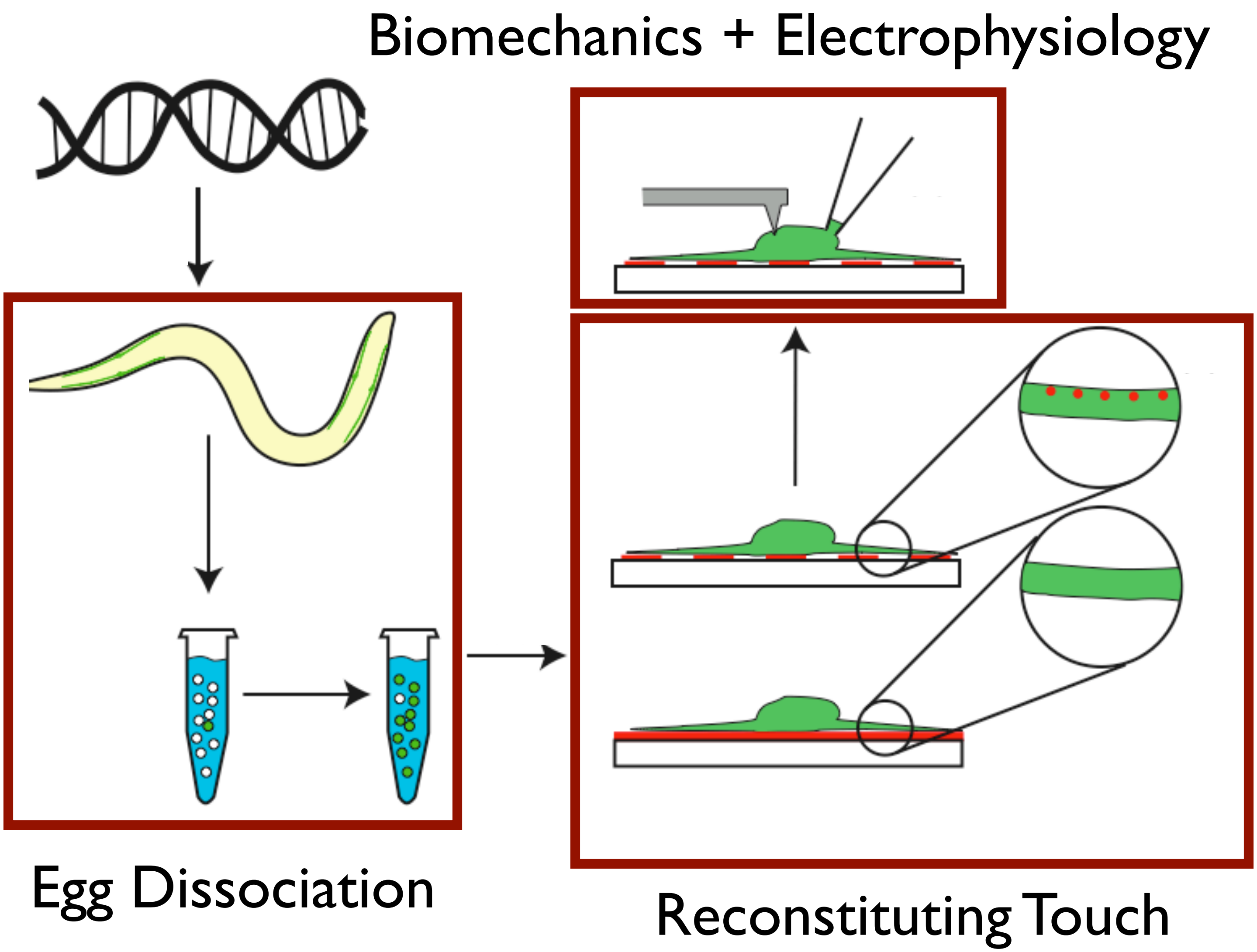
- 11M diabetics in US
- 59% suffer from Diabetic Peripheral Neuropathy (DPN)
- 66k lower limb amputations annually ($4.6-13.7B annually)



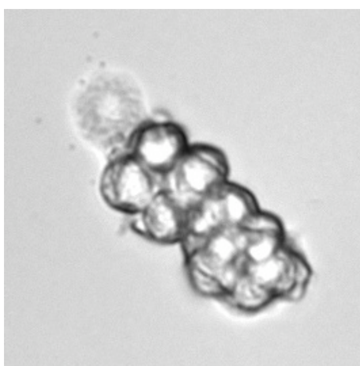
Gordois, A. et al. The Health Care Costs of Diabetic Peripheral Neuropathy in the U.S. Diabetes Care 26, 1790-1795 (2003).

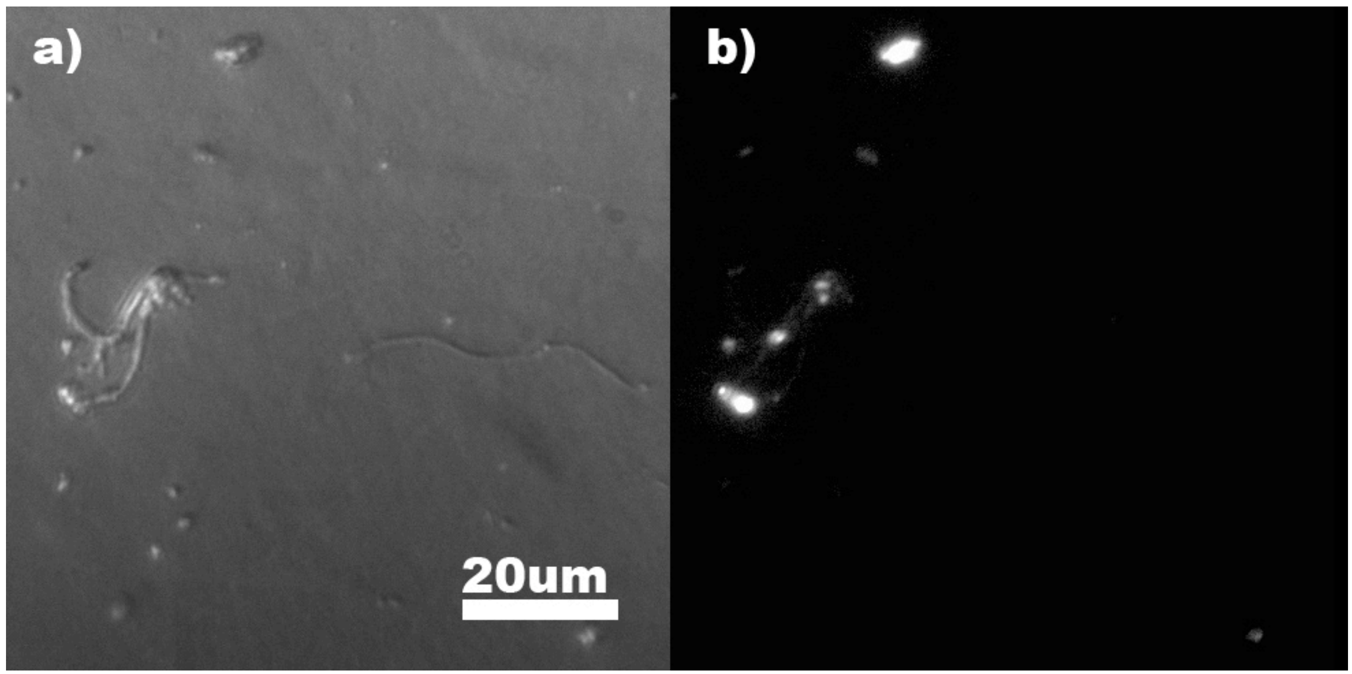
Planned Experiments

Planned Experiments

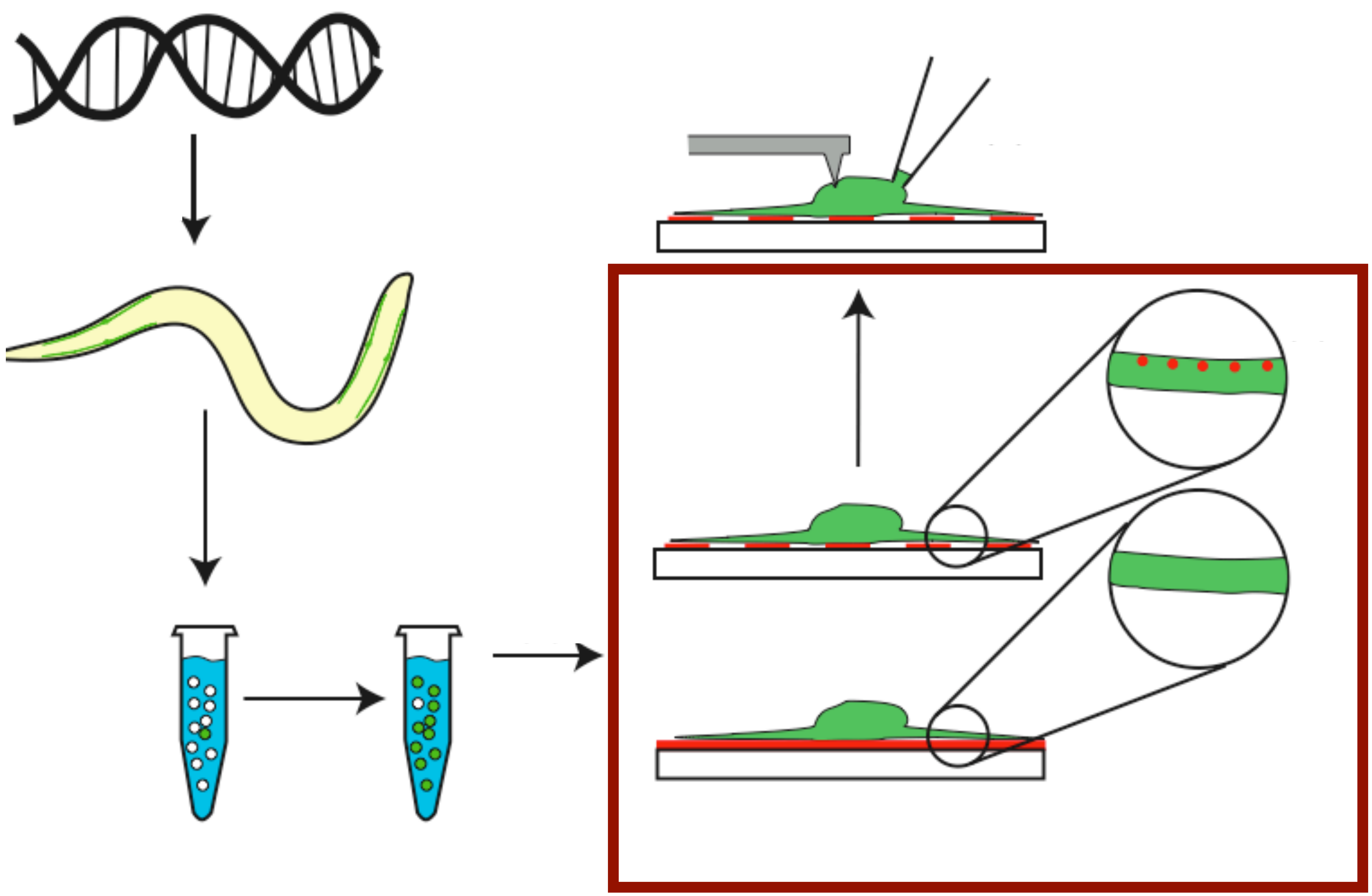


Obtaining Neurons



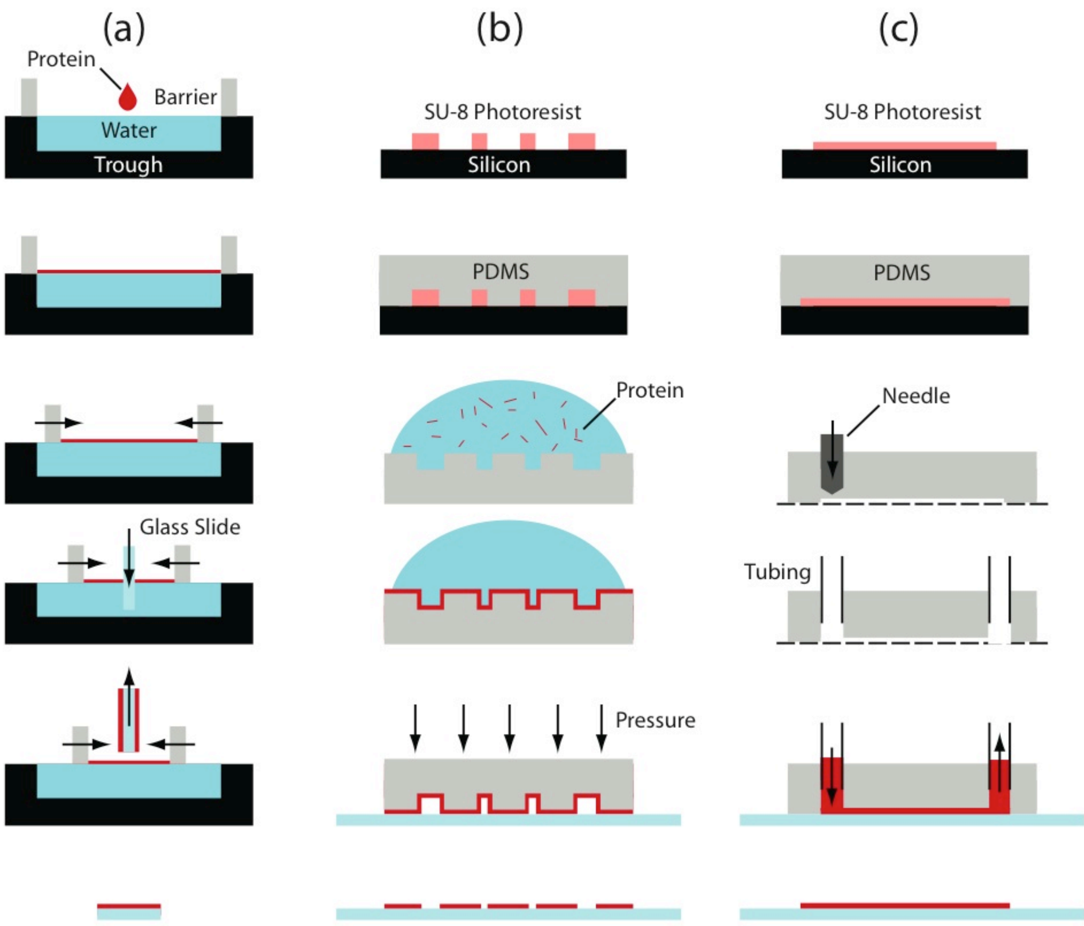


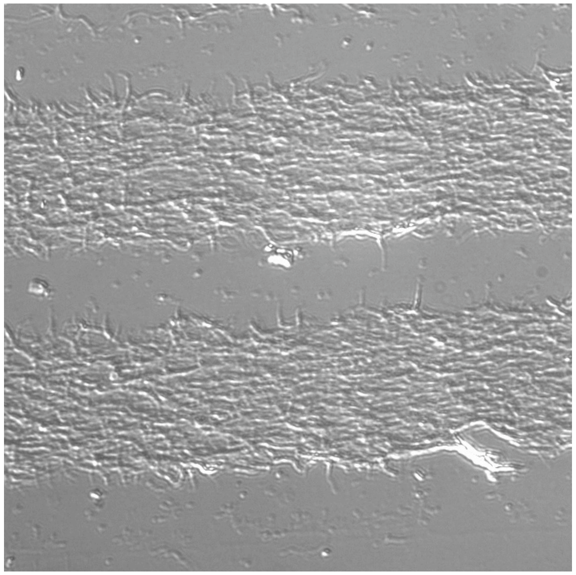
Planned Experiments



Reconstituting Touch

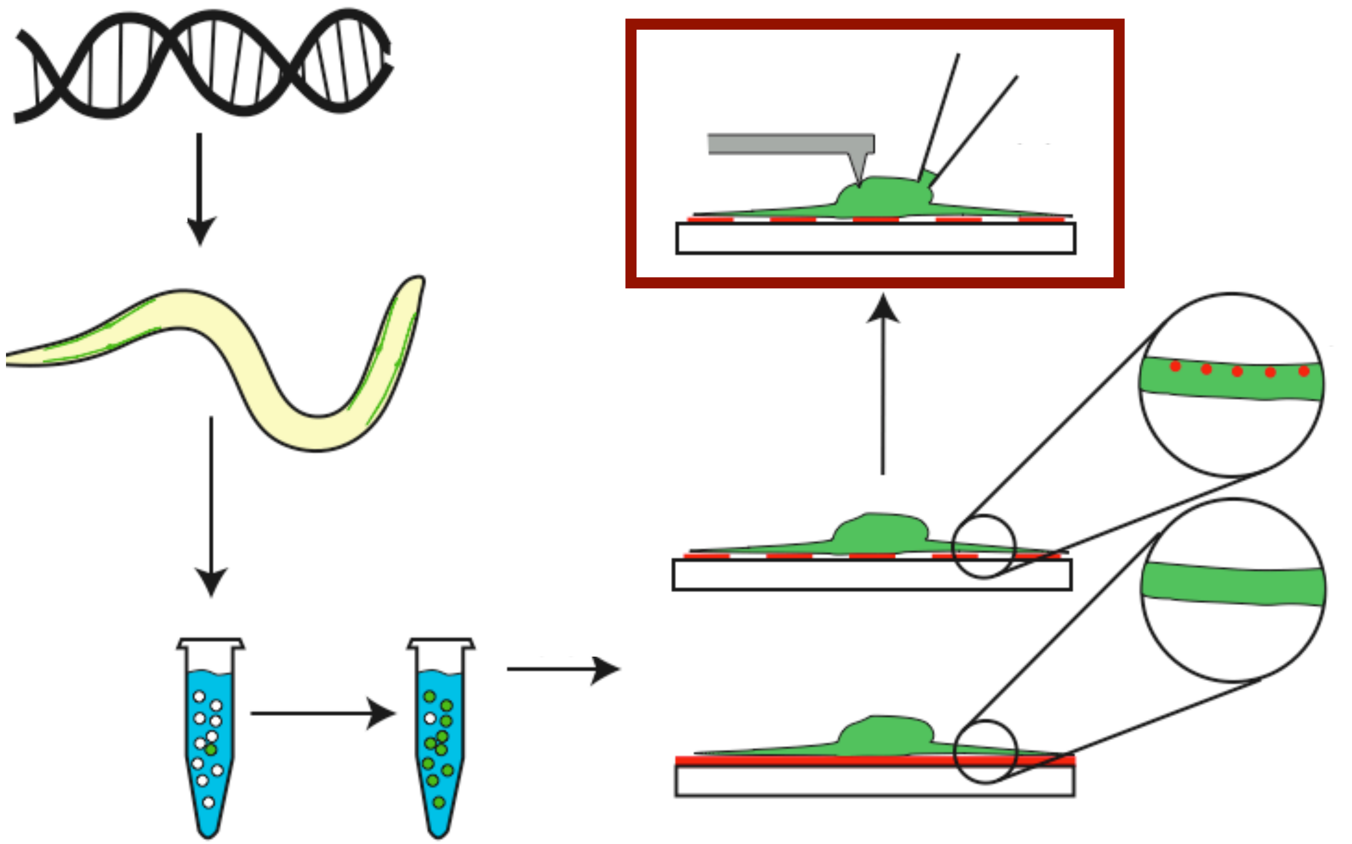
Reconstituting Touch



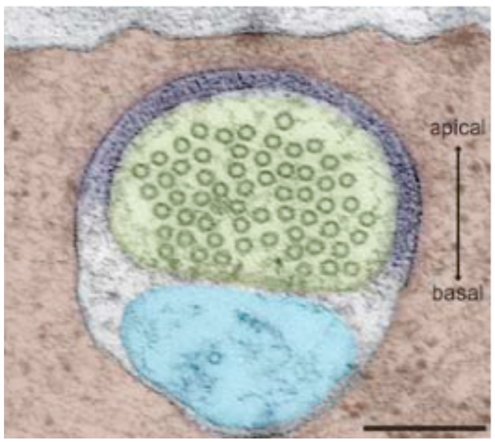


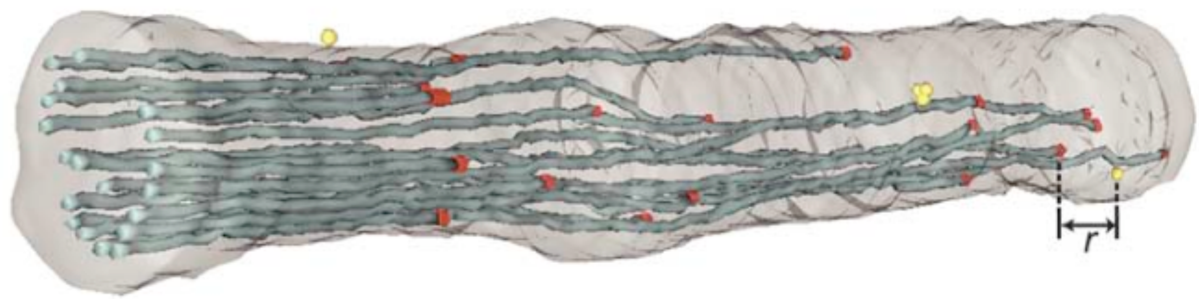
Planned Experiments

Cell Biomechanics



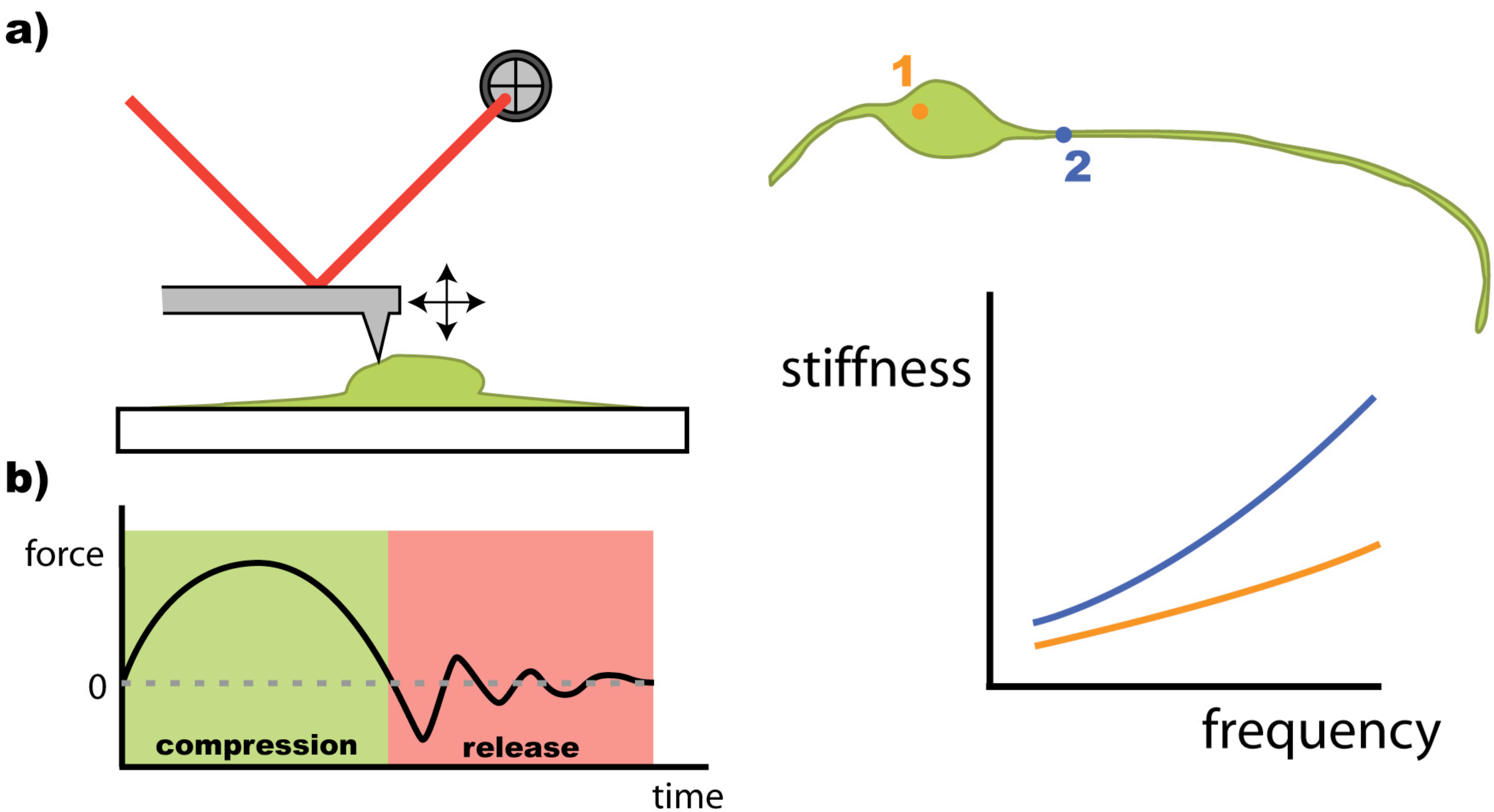
Biomechanics of Touch



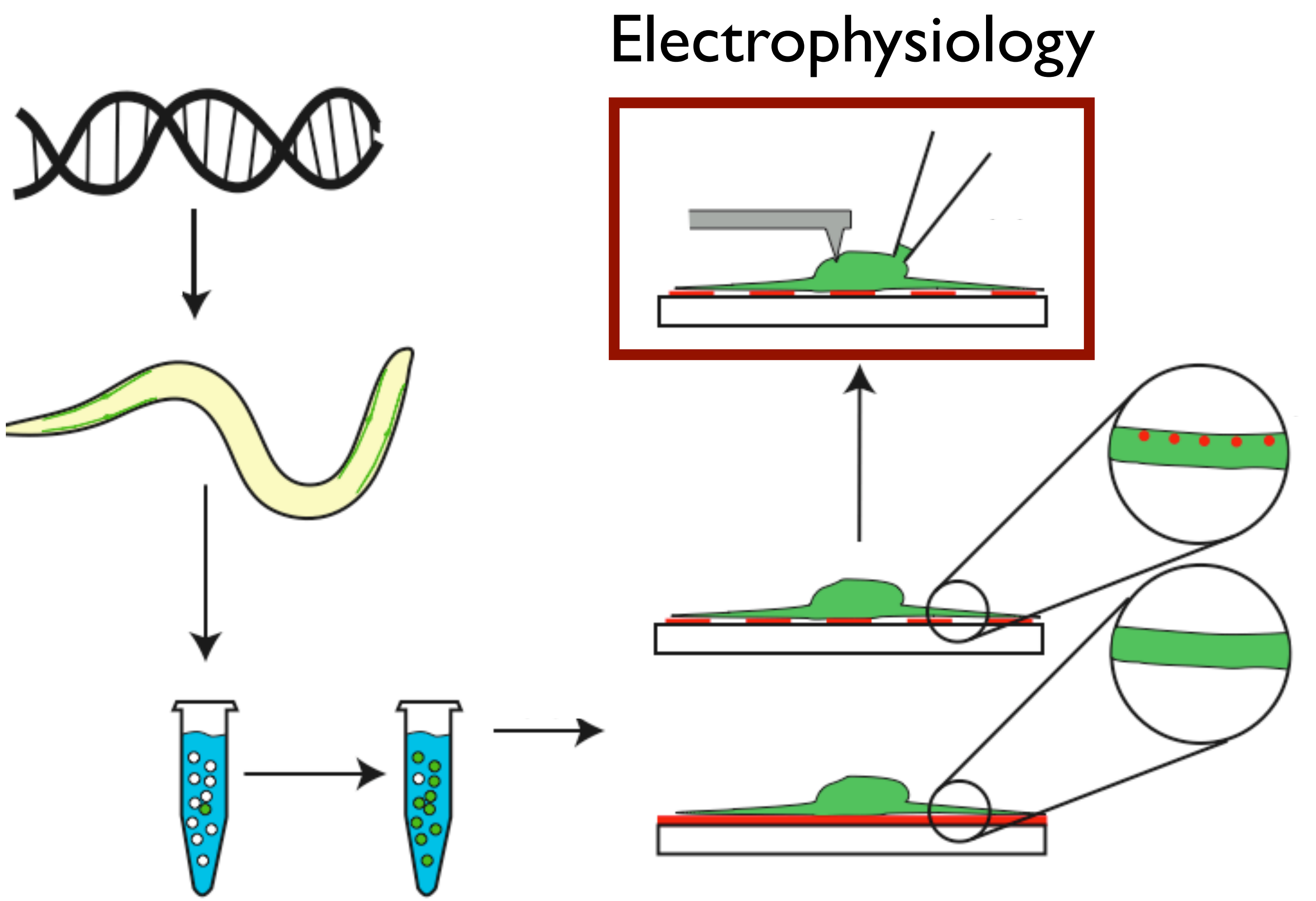


Nanoscale Organization of the MEC-4 DEG/ENaC Sensory
Mechanotransduction Channel in Caenorhabditis elegans
Touch Receptor Neurons, Juan G. Cueva, Atticus Mulholland, and Miriam B. Goodman, J. Neuroscience (2007)

Biomechanics of Touch



Planned Experiments



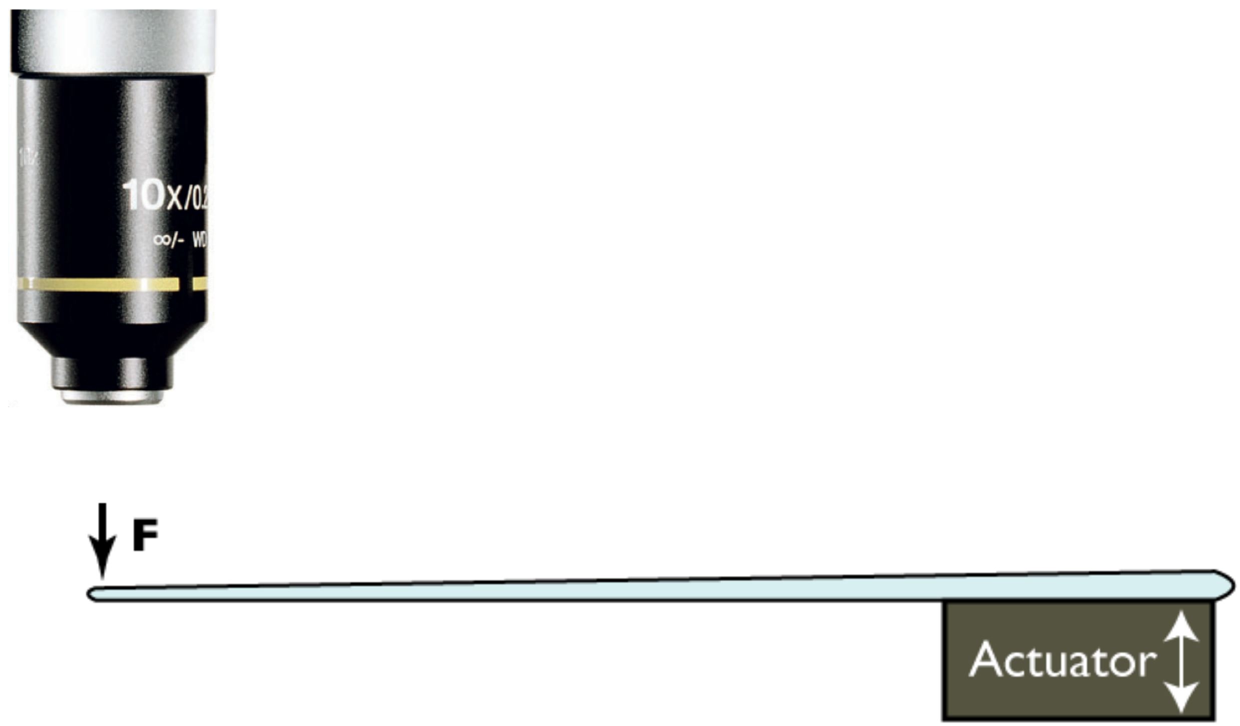
Design and Fabrication

Performance Targets

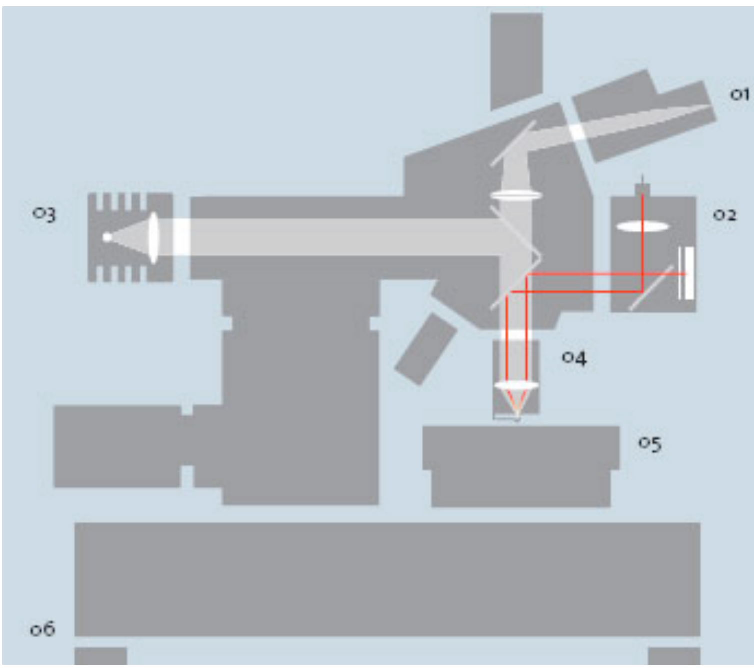
- Force resolution = 50pN
- Sensor bandwidth = 100kHz
- Actuator speed = 30us
- Closed loop force control

Covalent bond: 1600pN
Antibody-antigen: 100pN
Kinesin stall force: 6pN
Hydrogen bond: 4pN

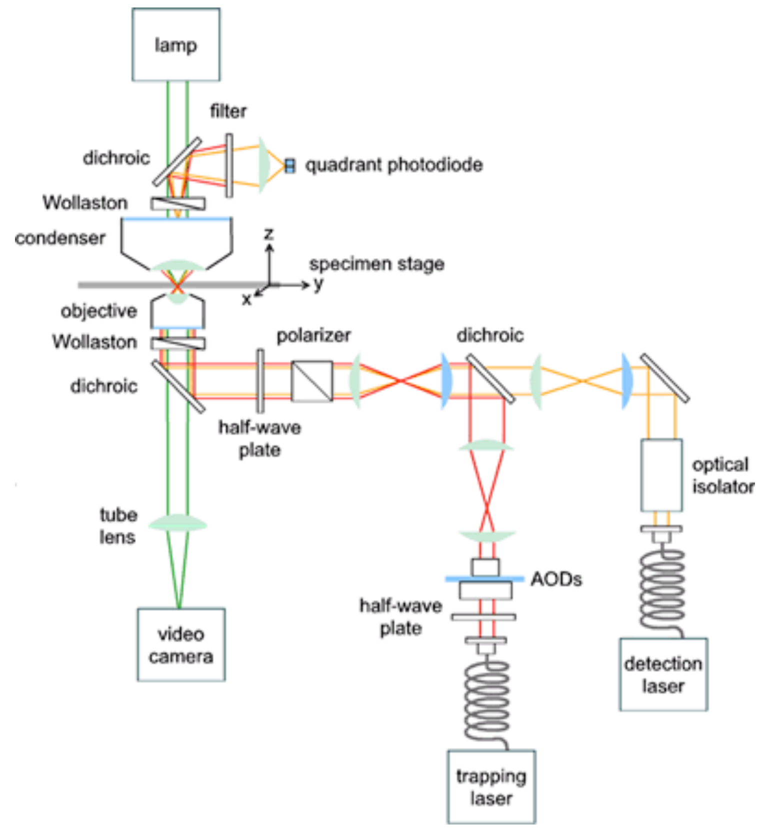
Current Technique



Other Techniques



Atomic Force Microscope

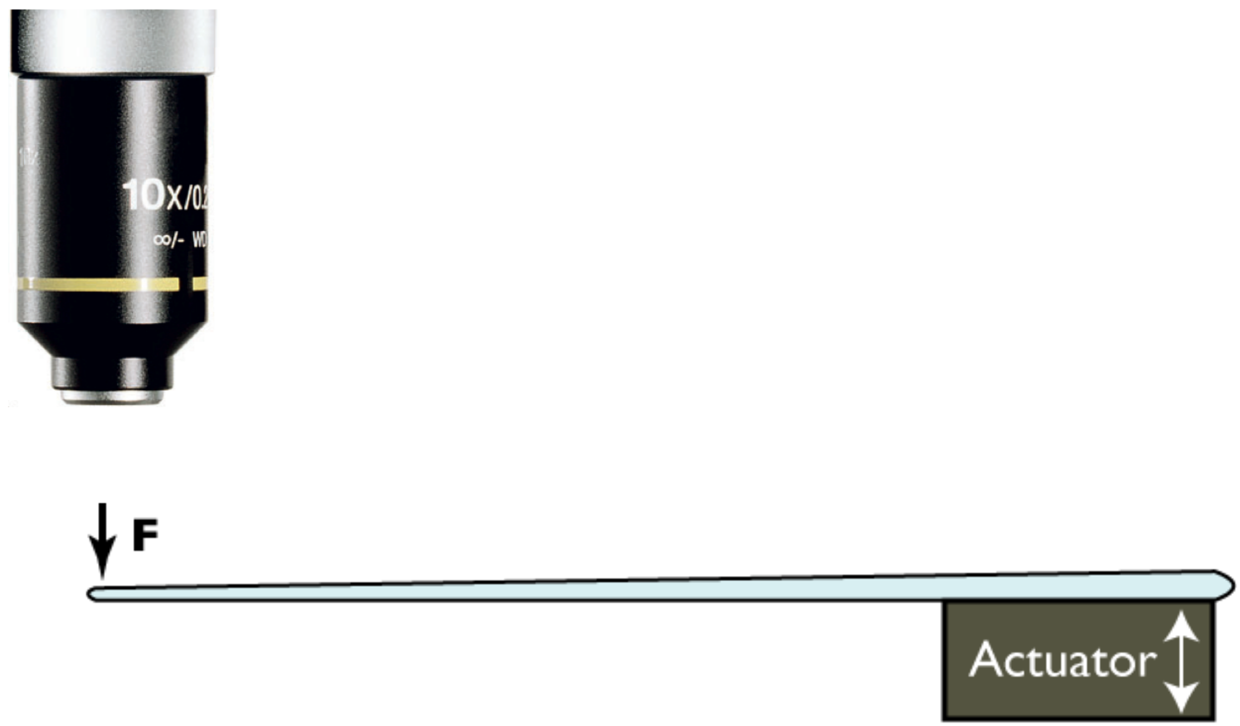


Optical Tweezers

http://www.witec.com

http://www.azonano.com/details.asp?ArticleID=1248

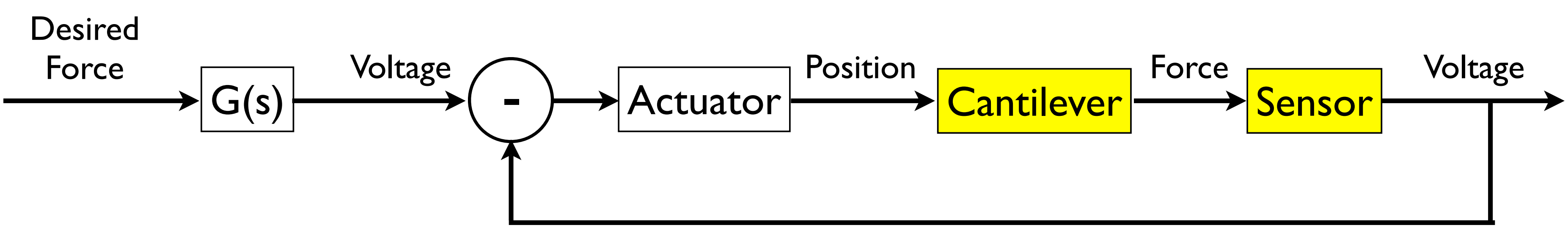
My Plans



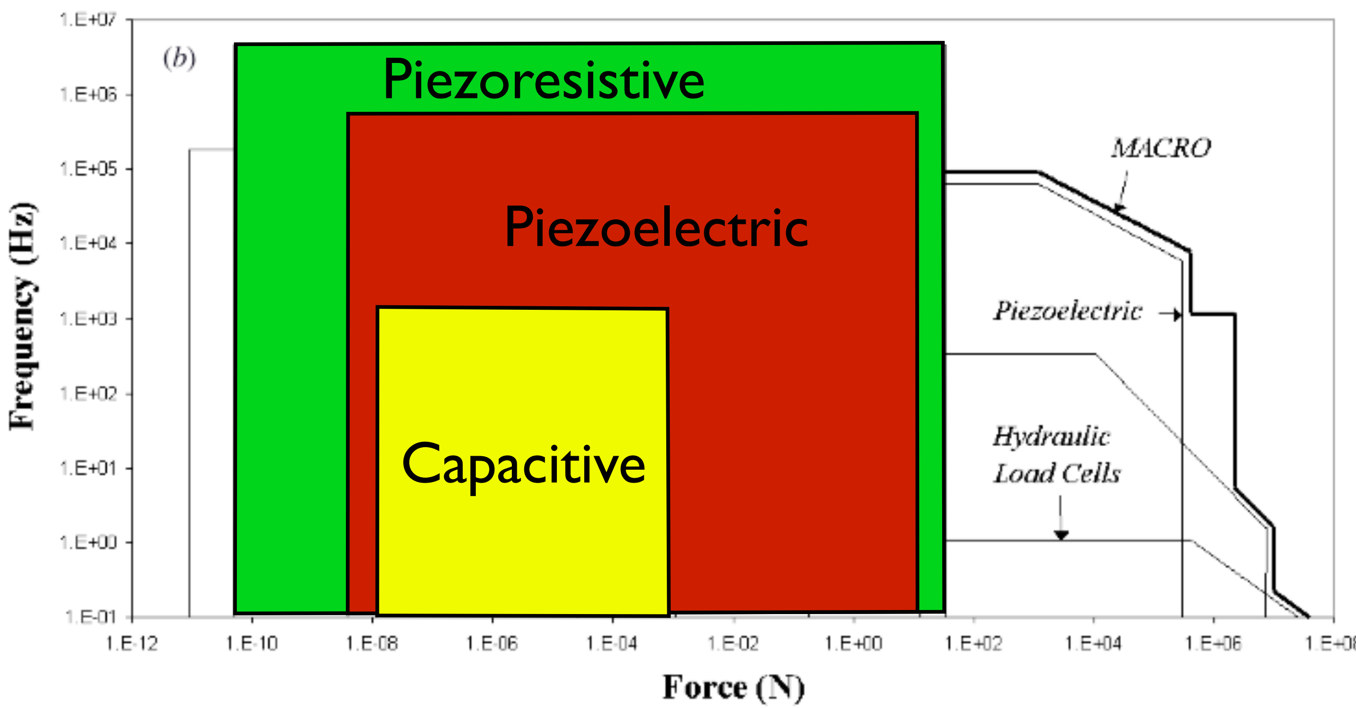
Why MEMS?

- Integrated sensor and actuator
- Electronic sensing and actuation
- Simple and inexpensive
- Performance
  - Force resolution ($k \sim L$)
  - Bandwidth ($f \sim 1/L$)

System Design



Sensor Selection



Bell D J, Lu T J, Fleck N A and Spearing S M 2005 MEMS actuators and sensors: observations on their performance and selection for purpose J. Micromech. Microeng. 15 S153–64

Sensor Selection

	Pros	**Cons**
Piezoresistive	-Best resolution -Simple circuit design	-Additional fabrication steps
Capacitive	-Sensor/actuator integration -Fabrication	-Small signal -Large sensor mass
Piezoelectric	-Sensor/actuator integration	-Noise -Exotic materials

Cantilever Design

Piezoresistivity $$\frac{\Delta R}{R} = G\varepsilon$$

Sensitivity $$\frac{\Delta V}{\Delta F} = V_i \frac{3G}{2E}\left(\frac{L}{wt^2}\right)$$

Resonant Frequency $$\omega = \sqrt{\frac{k}{m}} = \frac{\sqrt{E}t}{L^2}$$

Example (built)

S_J: $6\,\frac{\mathrm{nV}}{\sqrt{\mathrm{Hz}}}$

Sensitivity: $610\,\frac{\mathrm{N}}{\mathrm{V}}$

F_{res}: $10\,\frac{\mathrm{pN}}{\sqrt{\mathrm{Hz}}}$

F_{min}: $3\mathrm{nN}$

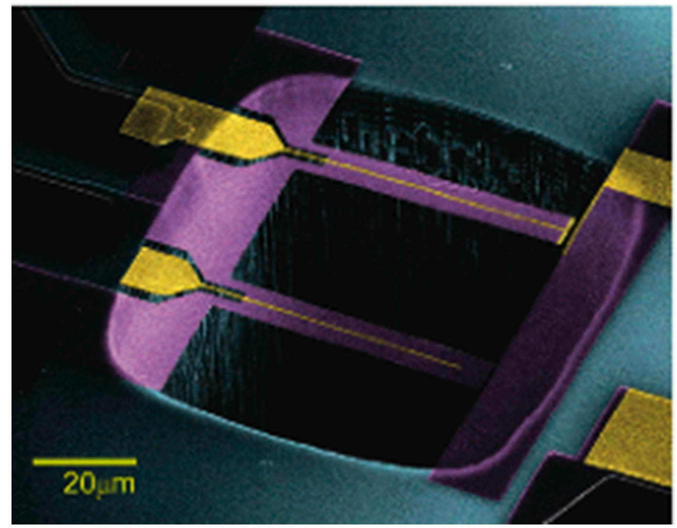
Piezoresistor Noise

Sensitivity vs Noise

Johnson Noise $S_J = 4k_bTR$

1/f Noise $S_{1/f} = \frac{V_b^2\alpha}{Nf}$

Brownian Noise $S_F = 4k_bT\gamma_{eff}$



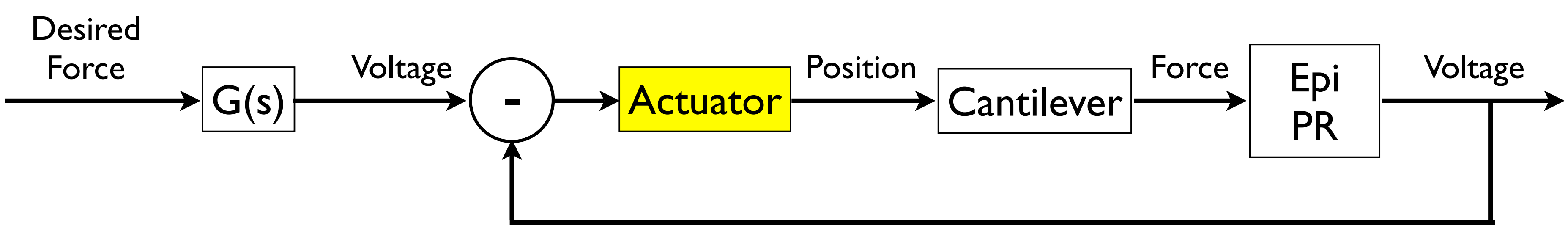
235 aN/rtHz @ 58 kHz

Self-Sensing Micro- and Nanocantilevers with Attonewton-Scale Force Resolution, Arlett et al., Nano Letters (2006)

Piezoresistor Fabrication

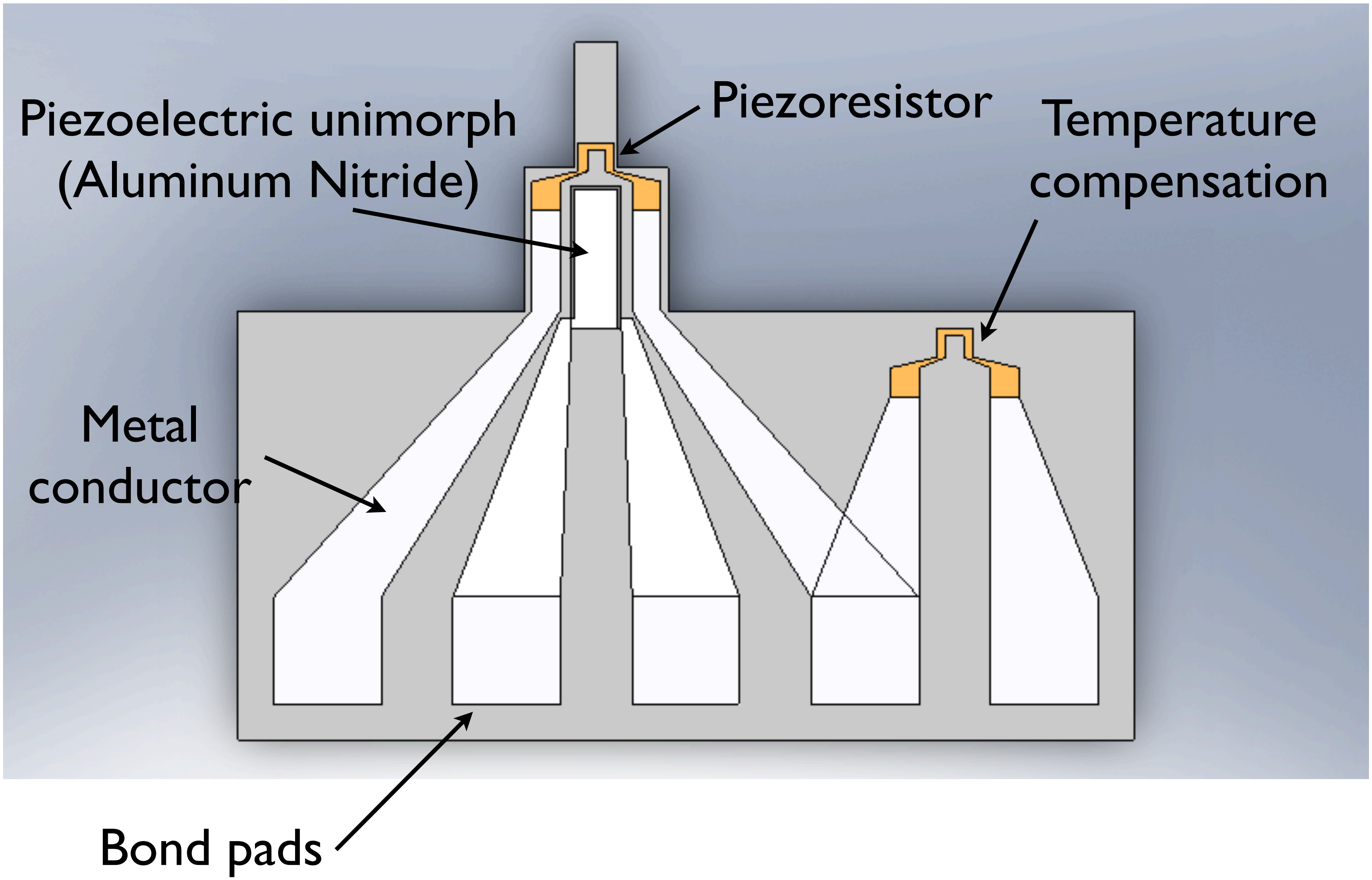
	Pros	**Cons**
Ion implantation	-Widely used -Well characterized	-Junction depth
Epitaxy	-Shallow junction -Well characterized	-Equipment
Diffusion	-Shallow junction	-Rarely used -Reliability

System Design

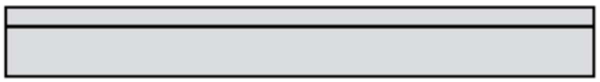


Actuation

	Pros	Cons
Piezoelectric	-Low voltage -Straightforward control	-Additional fabrication steps
Electrostatic	-Standard materials, fabrication -Widely used	-Sample heating -High voltage -Driving circuit
Magnetic		-Partly off-chip -Does not scale to cantilever arrays -Exotic materials
Thermal		-Low frequency -Temperature gradients


Piezoelectric unimorph
(Aluminum Nitride)
Piezoresistor
Temperature
compensation
Metal
conductor
Bond pads

Process



n-type Si

p-type Si

SiO_2

Pt/Ti

AlN

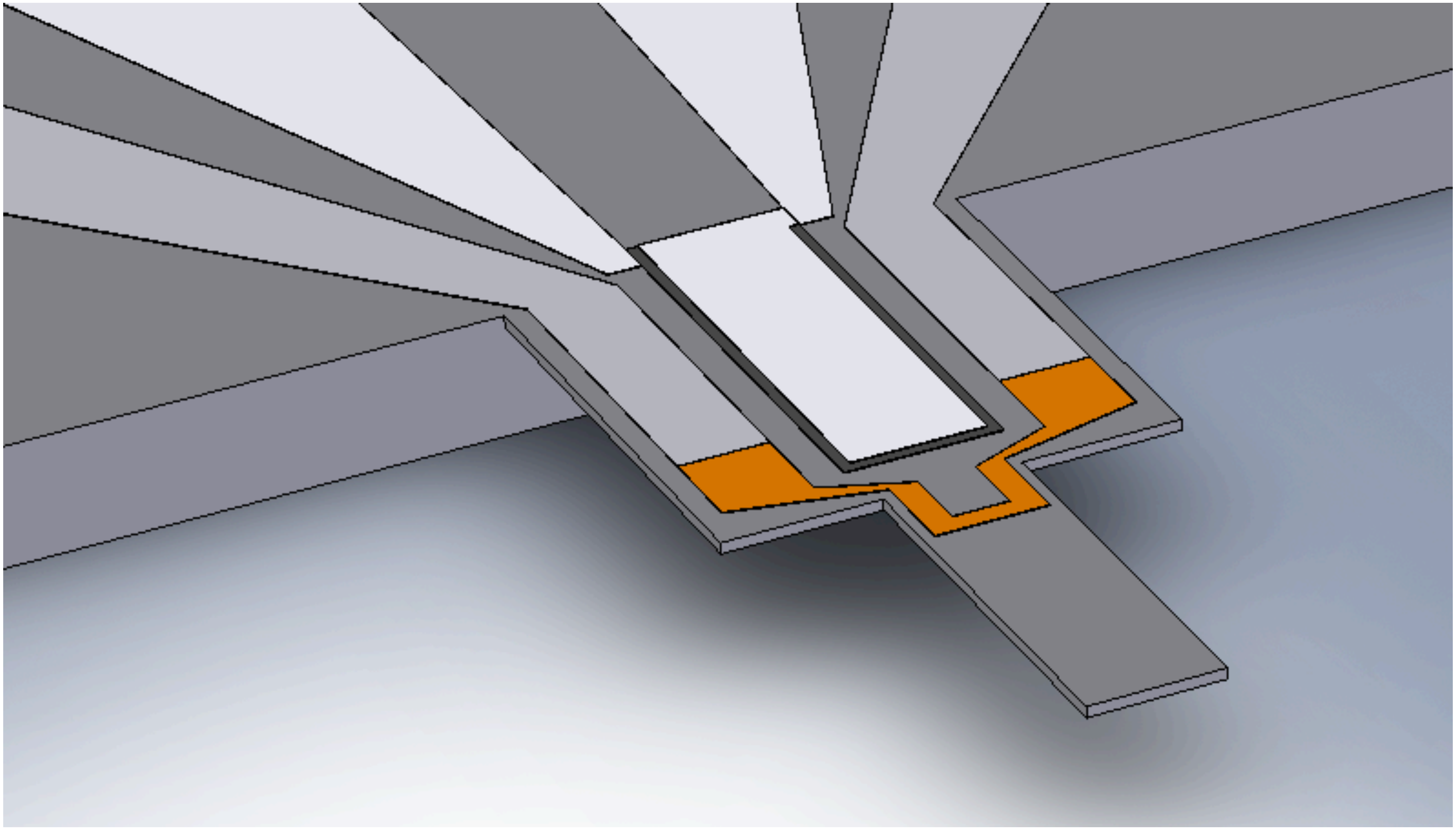
Al

Conclusion

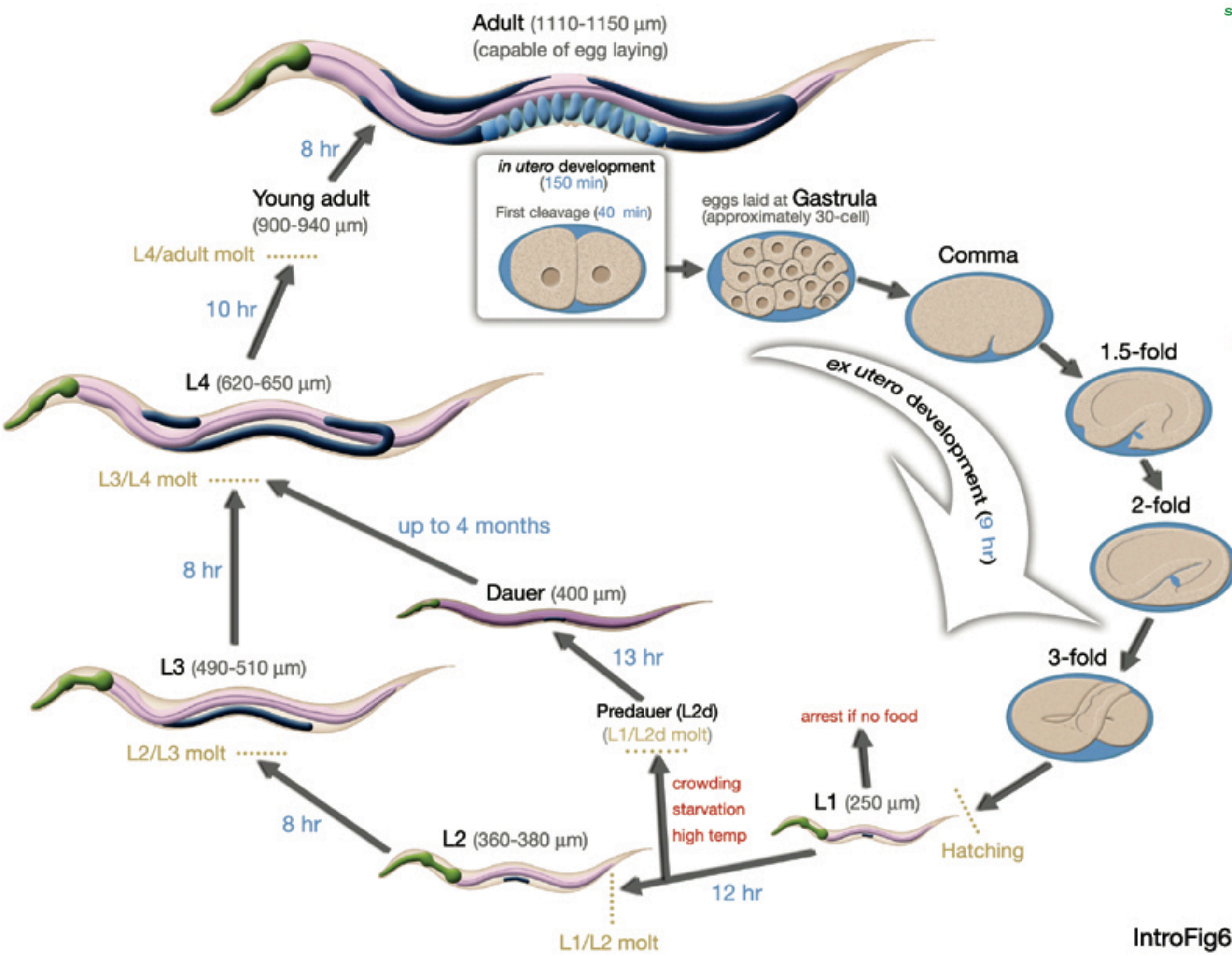
- MEMS sensor and actuator for applying pN - nN scale forces with microsecond time resolution
- Enable new biological measurements with atomic scale force resolution
- Plan to study mechanically gated ion channels at the single cell level

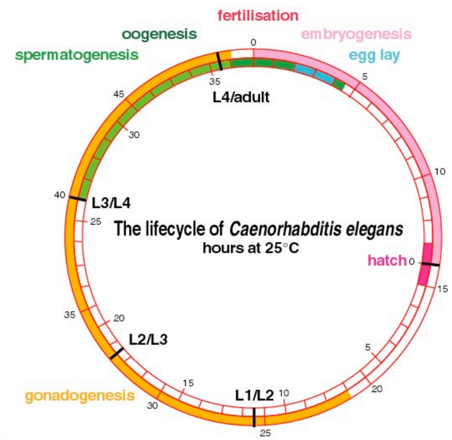

Thank You.
Questions?

[redacted]



Why C. elegans?

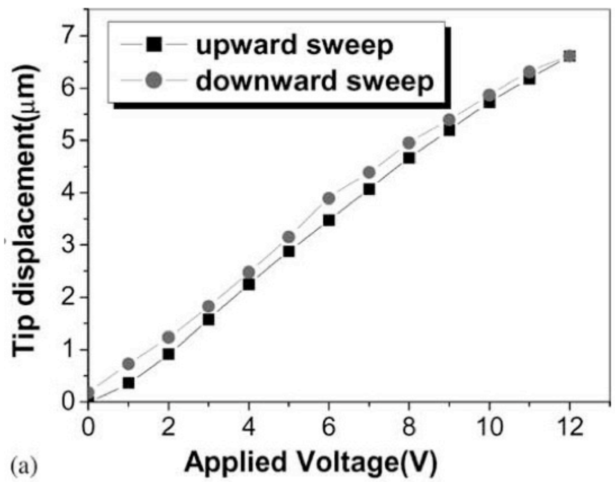


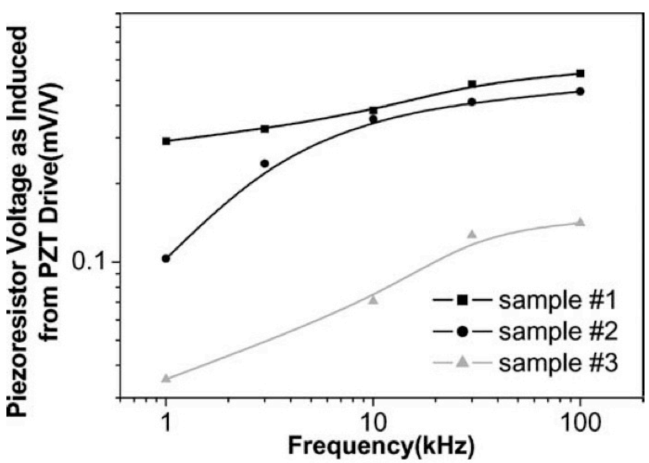


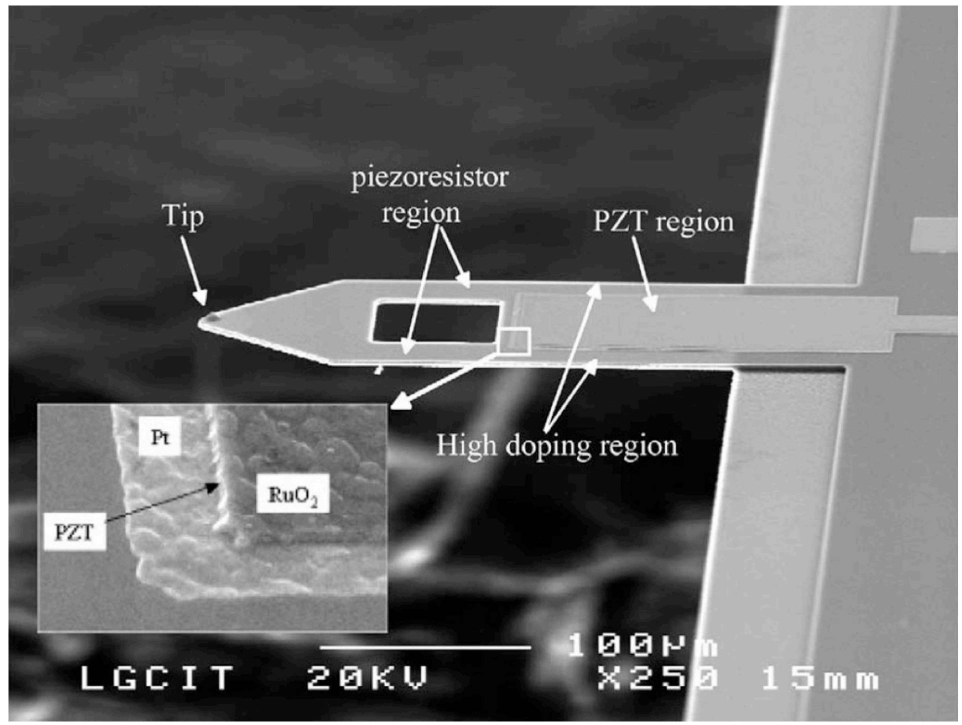
Jorgensen, E. M. & Mango, S. E. THE ART AND DESIGN OF GENETIC SCREENS: CAENORHABDITIS ELEGANS. Nature Reviews Genetics 3, 356-369 (2002).

http://www.wormatlas.org

Previous Work





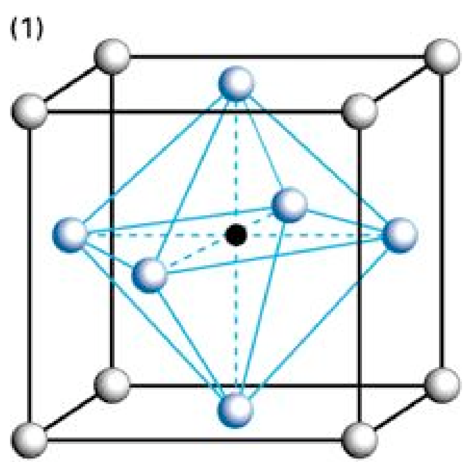


~10 references on integrated piezoelectric actuation + piezoresistive sensing

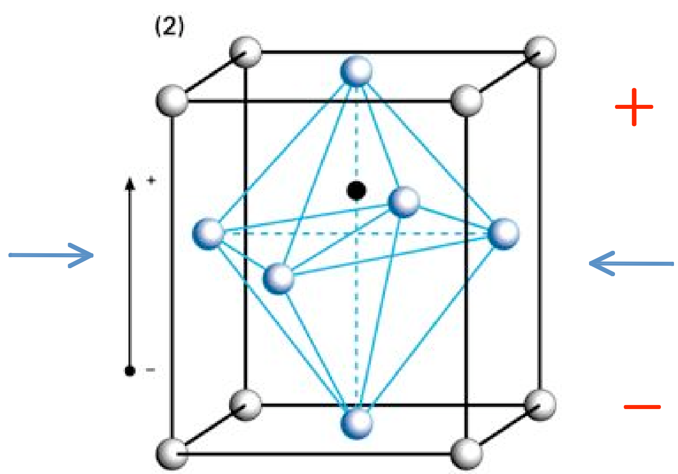
PZT

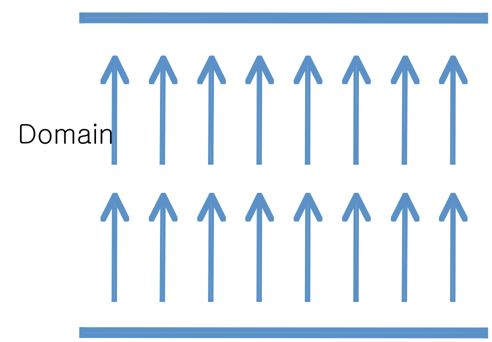
- Perovskite Structure (ABX3)
  - A=Pb, B=Ti, X=O
  - Zirconium as dopant of Pb
  - Stochiometry Pb:Zr:Ti = 1:0.52:0.48

ALD, Sputtering, Sol-gel



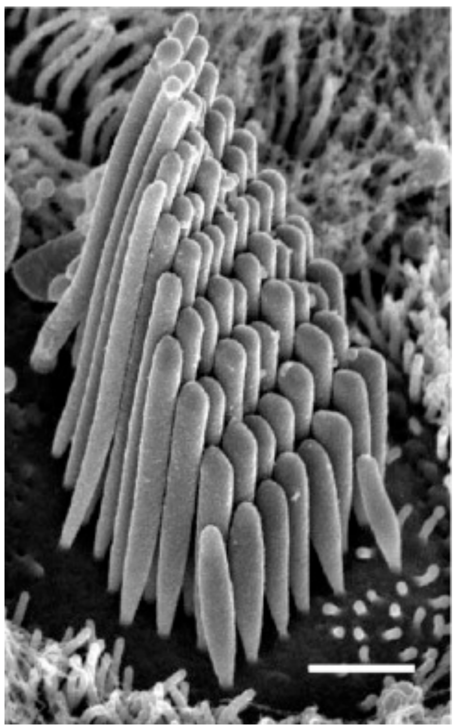
A : Body Center (Pb : Large)
B : Face Center (Ti : Small)
X : Every corner (Oxygen)



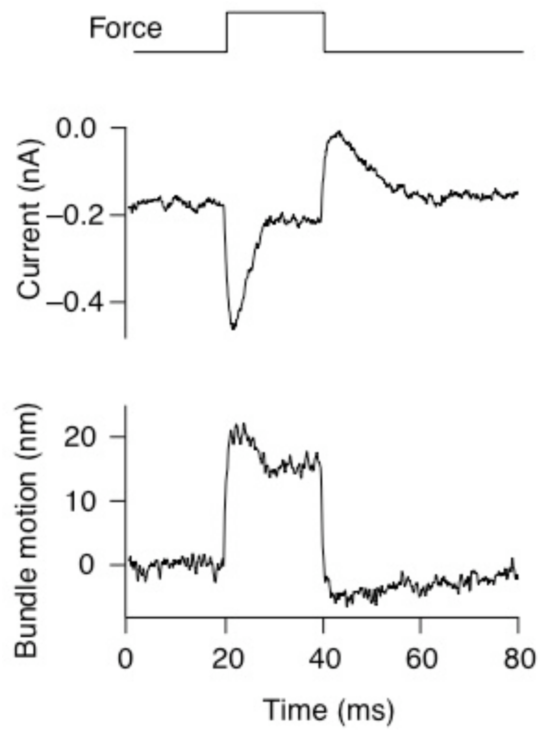


The position change of A makes the cell polarized. After heat treatment (Curie temperature), the domain (or grain, composed of cells) has a ferromagnetic (or ferroelectric) which makes the material have a different electrical conductivity.

Cochlear Hair Cells

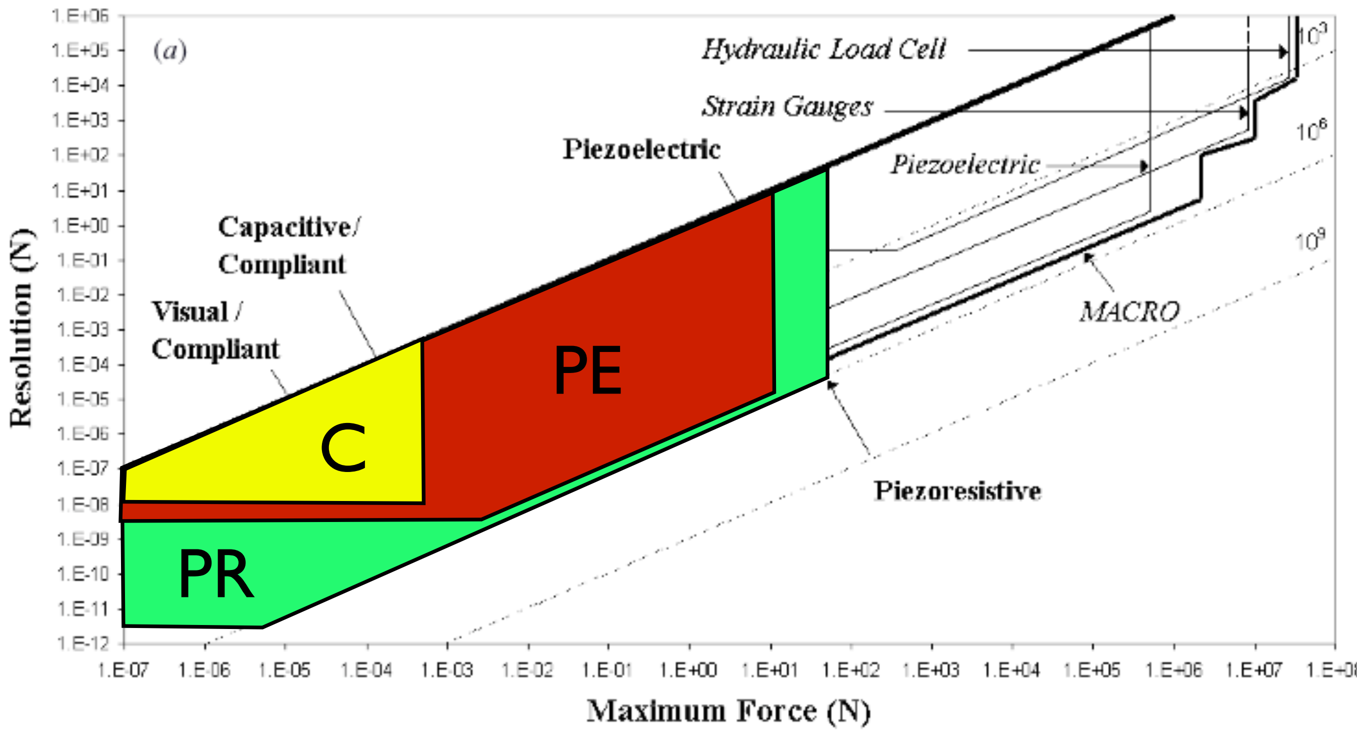


R. Fettiplace,A. J.Ricci and C. M.Hackney, Clues to the cochlear amplifier from the turtle ear, Trends in Neuroscience (2001)



A. J. Ricci,A. C. Crawford,and R. Fettiplace, Active Hair Bundle Motion Linked to Fast Transducer Adaptation in Auditor y Hair Cells, J. Neuroscience (2000)

Sensor Selection



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Constitutive Equations

$$\underbrace{S}_{\text{strain}} = \overbrace{s^E}^{\text{compliance}} \underbrace{T}_{\text{stress}} + \overbrace{d^{Tr}}^{\text{piezoelectric strain coefficients (transpose)}} \underbrace{E}_{\text{electric field}}$$

$$\underbrace{D}_{\text{electric displacement}} = \overbrace{d}^{\text{piezoelectric strain coefficients (transpose)}} \underbrace{T}_{\text{stress}} + \overbrace{\varepsilon^T}^{\text{dielectric permittivity}} \underbrace{E}_{\text{electric field}}$$

Superscripted material constants (e.g. s^E) are those values obtained when the superscripted quantity is held constant.

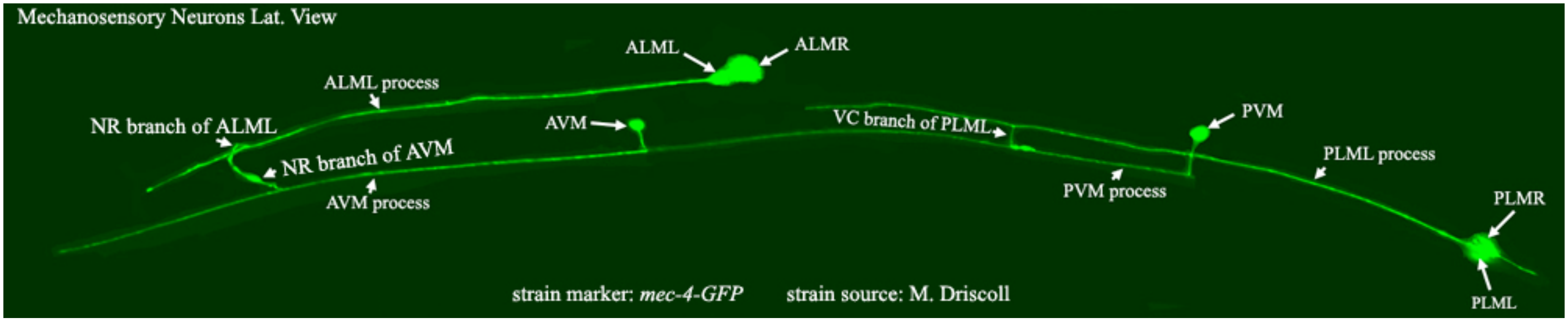
Piezoelectric Materials

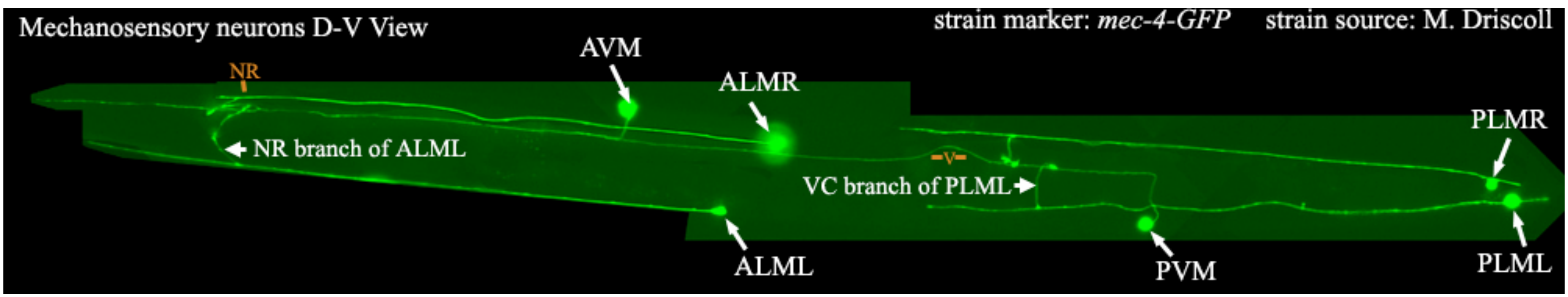
	Modulus (GPa)	d_{33} (pC/N)	Density (kg/m^3)	Residual Stress (MPa)
Aluminum Nitride (AlN)	330	5.6	3260	
PZT ($PbZrTiO3$)	48-135	190	7550	100
Zinc Oxide (ZnO)	210	10	5600	

(all data for thin films)

A little tensile stress not a bad thing

Neurons

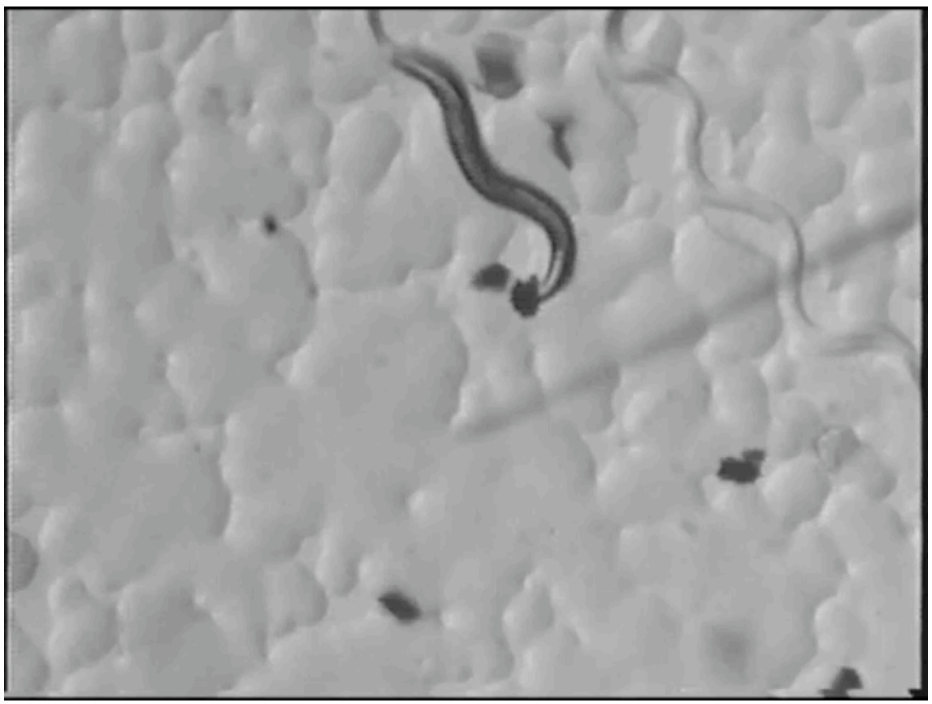




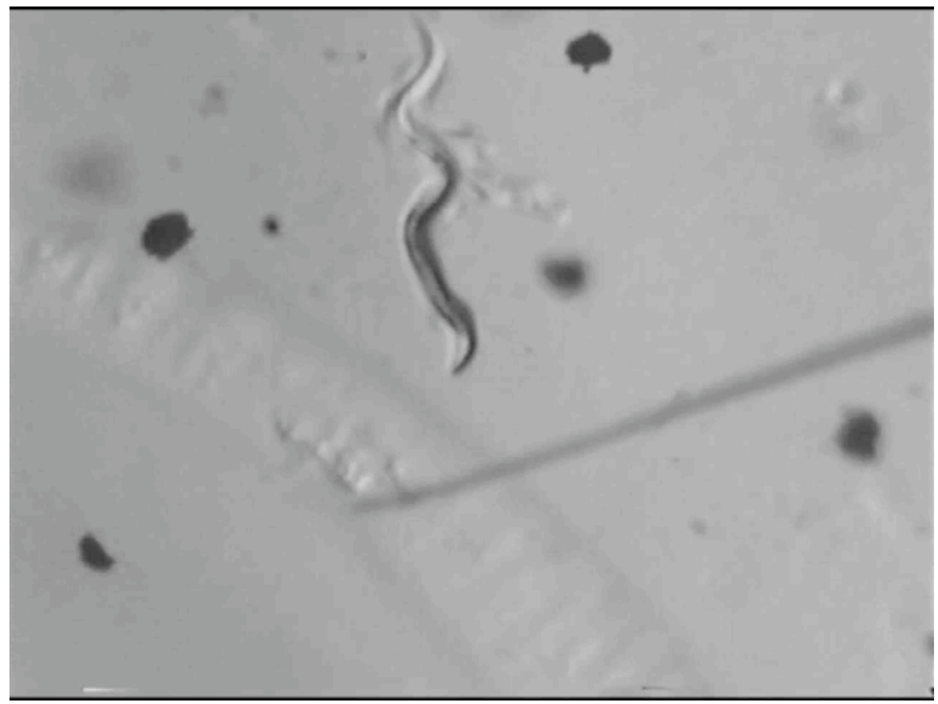
AVM, PVM, ALML/R, PLML/R

http://www.wormatlas.org/cellid/bodymechsen.htm

Mechanotransduction at Work

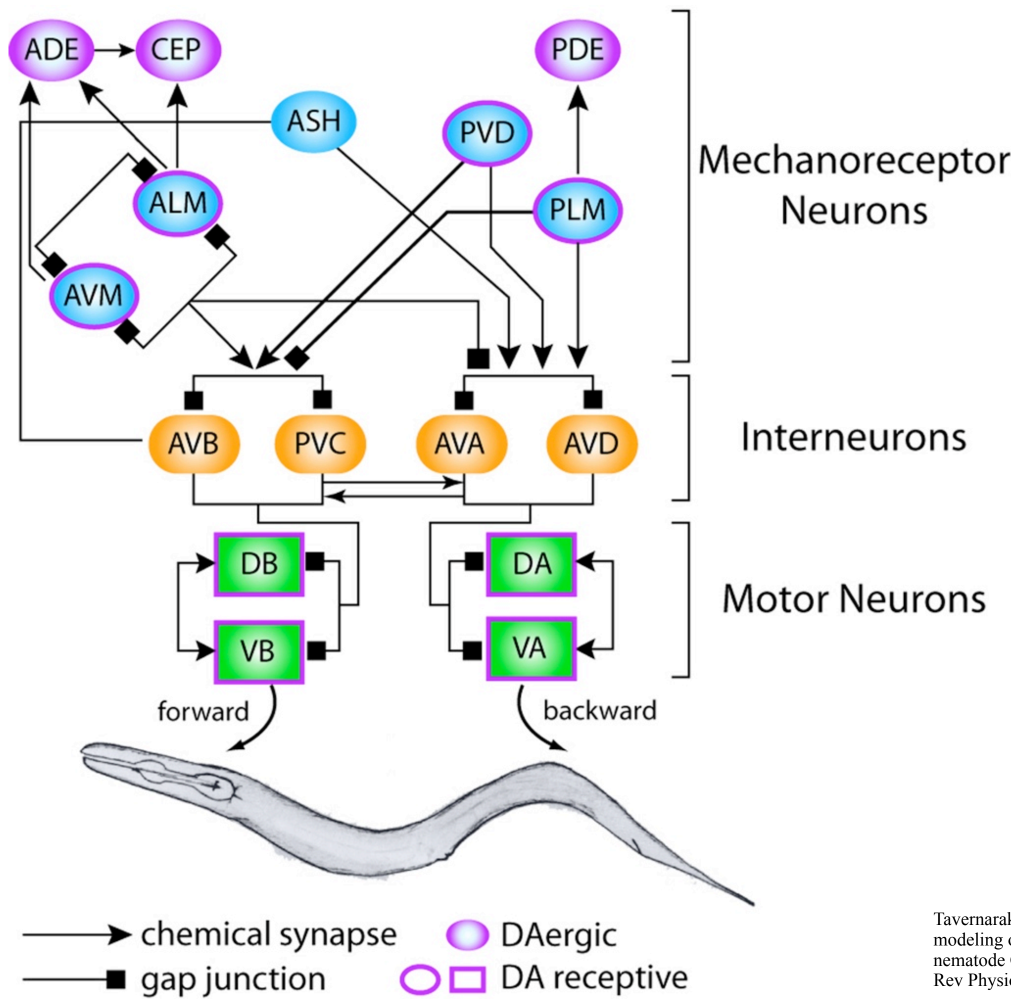


wildtype



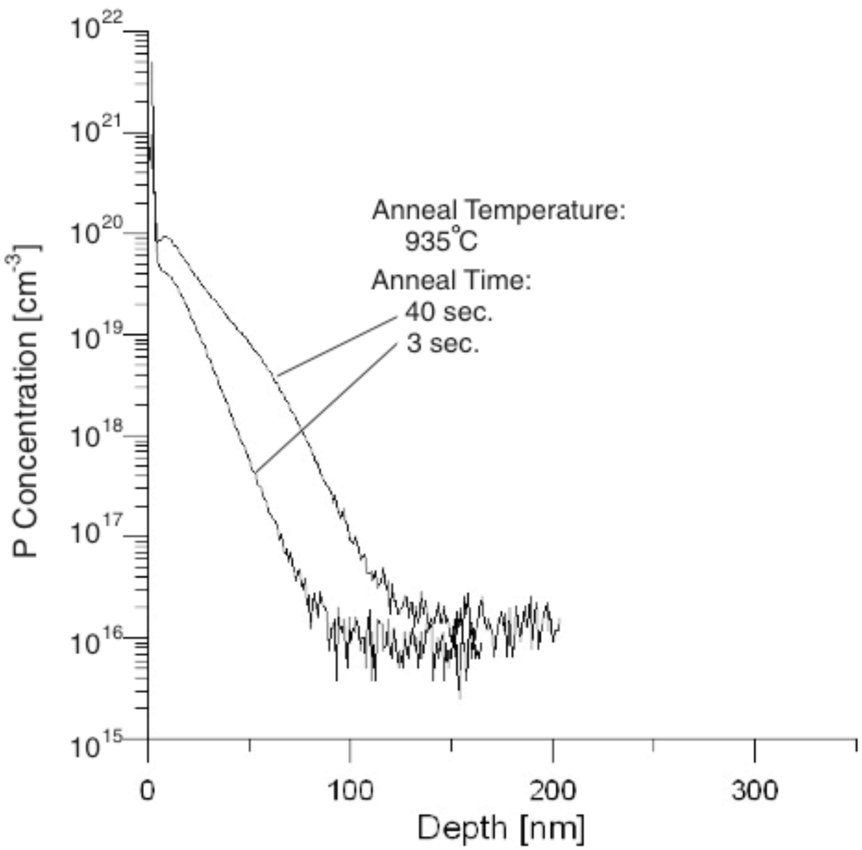
osm-9

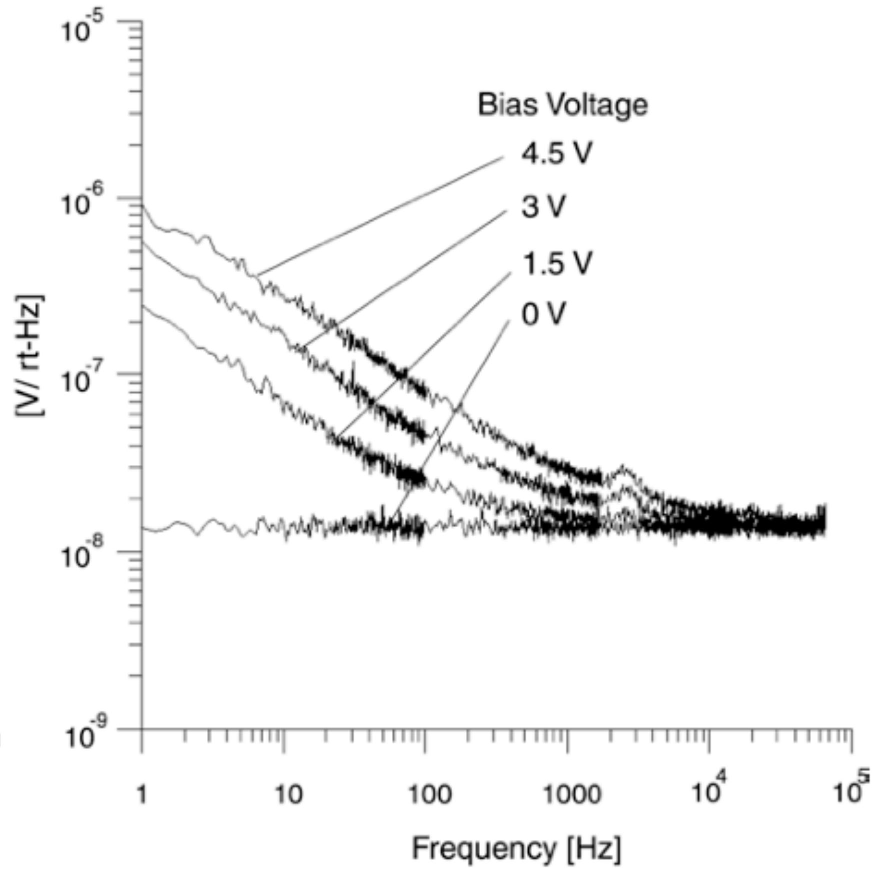
Neurons



Tavernarakis, N. & Driscoll, M. Molecular modeling of mechanotransduction in the nematode Caenorhabditis elegans. Annu Rev Physiol 59, 659-89 (1997).

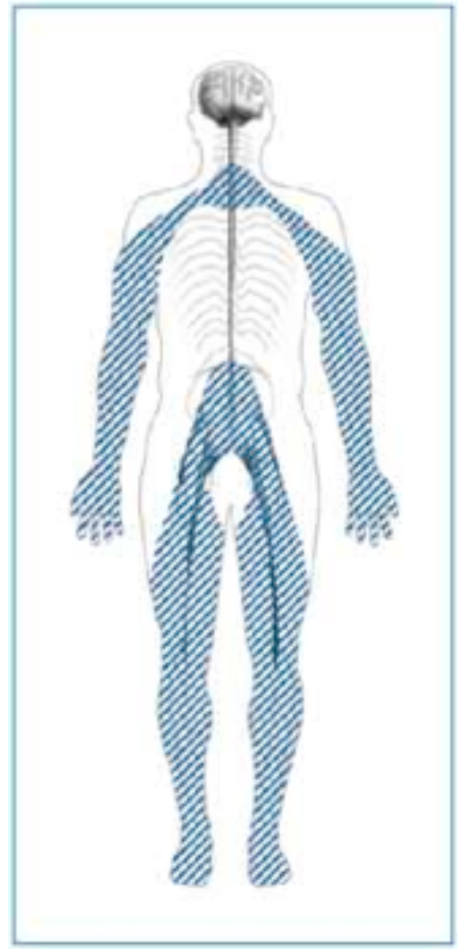
Diffused Cantilevers





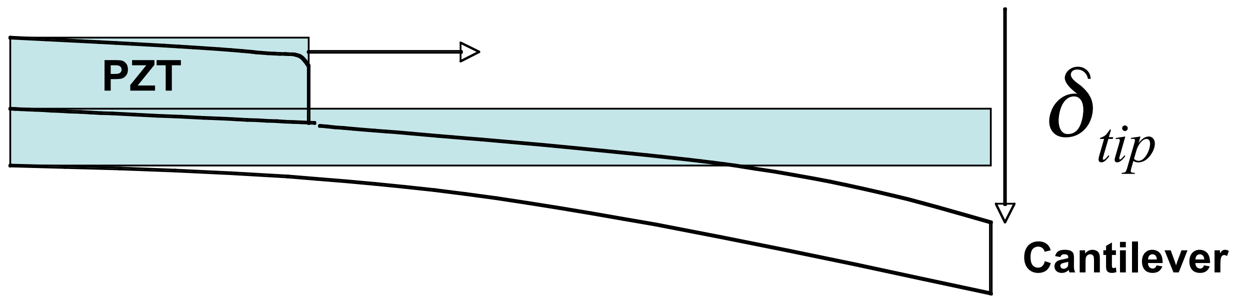
Clinical Impact

- 11M diabetics in US
- 59% suffer from Diabetic Peripheral Neuropathy (DPN)
- 66k lower limb amputations annually ($4.6-13.7B annually)



Gordois, A. et al. The Health Care Costs of Diabetic Peripheral Neuropathy in the U.S. Diabetes Care 26, 1790-1795 (2003).

Piezoelectric Unimorph



$s_{longitudinal}$ Strain of PZT in longitudinal direction

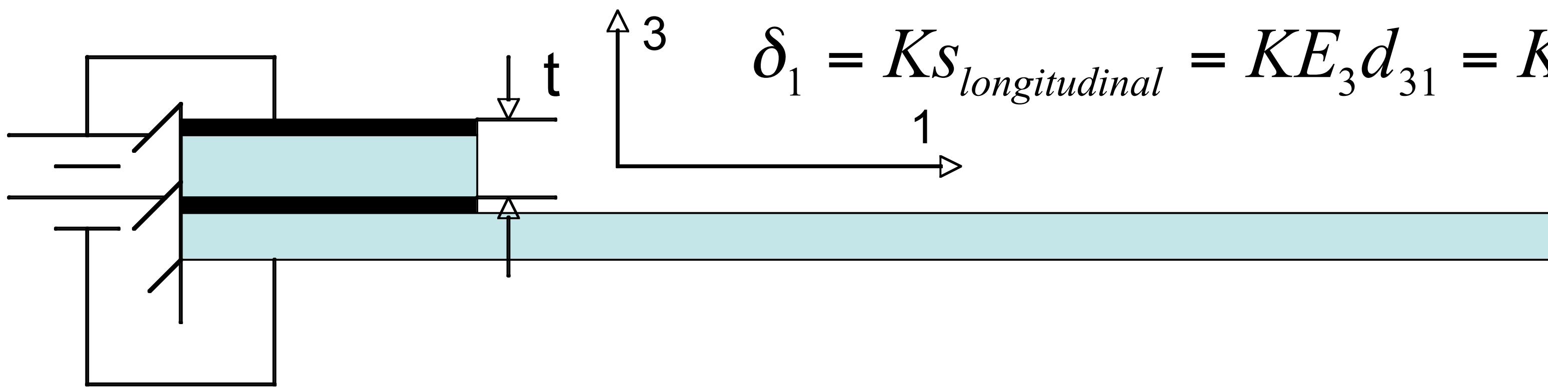
δ_{tip} Vertical displacement of cantilever tip

It is found that: $\delta_{tip} = K s_{longitudinal}$

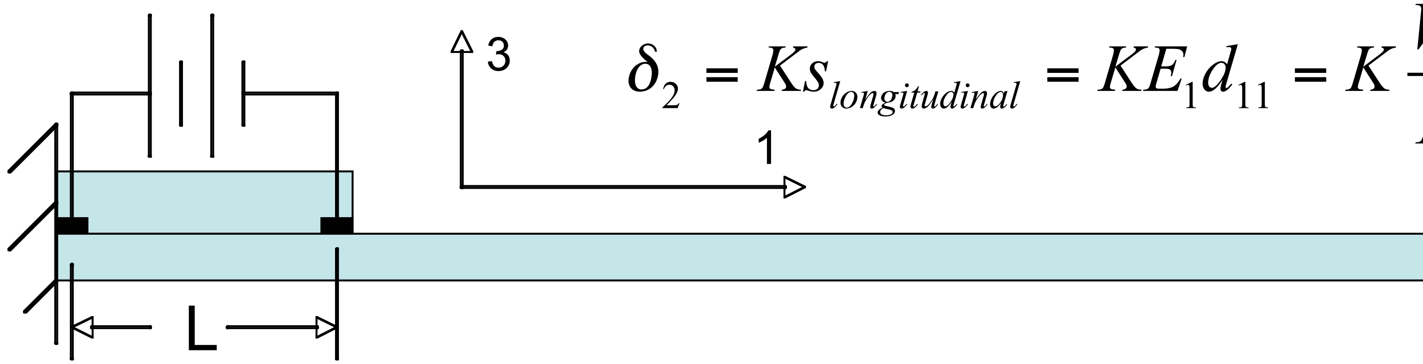
where stiffness coefficient is given by:

$$K = \frac{2(t_p + t_e)(A_p E_p A_e E_e)}{4(A_e E_e + A_p E_p)(E_p I_p + E_e I_e) + (t_e + t_p)^2 A_p E_p A_e E_e}$$

Piezoelectric Unimorph

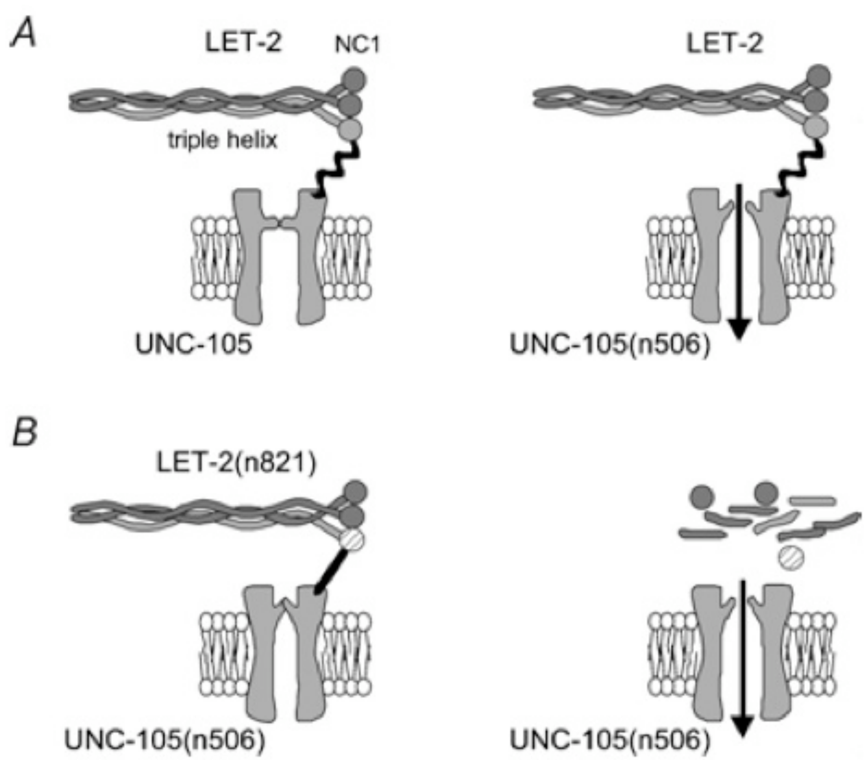


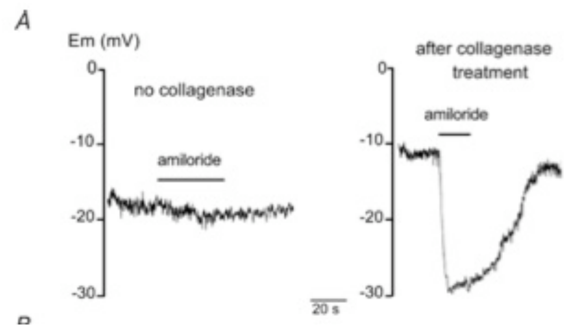
$$\delta_1 = Ks_{longitudinal} = KE_3 d_{31} = K\frac{V}{t}d_{31}$$



$$\delta_2 = Ks_{longitudinal} = KE_1 d_{11} = K\frac{V}{L}d_{11}$$

Extracellular Linkages





Jospin, M., Mariol, M. C., Segalat, L. & Allard, B. Patch clamp study of the UNC-105 degenerin and its interaction with the LET-2 collagen in Caenorhabditis elegans muscle. J Physiol 557, 379-88 (2004).

Reconstituting Touch