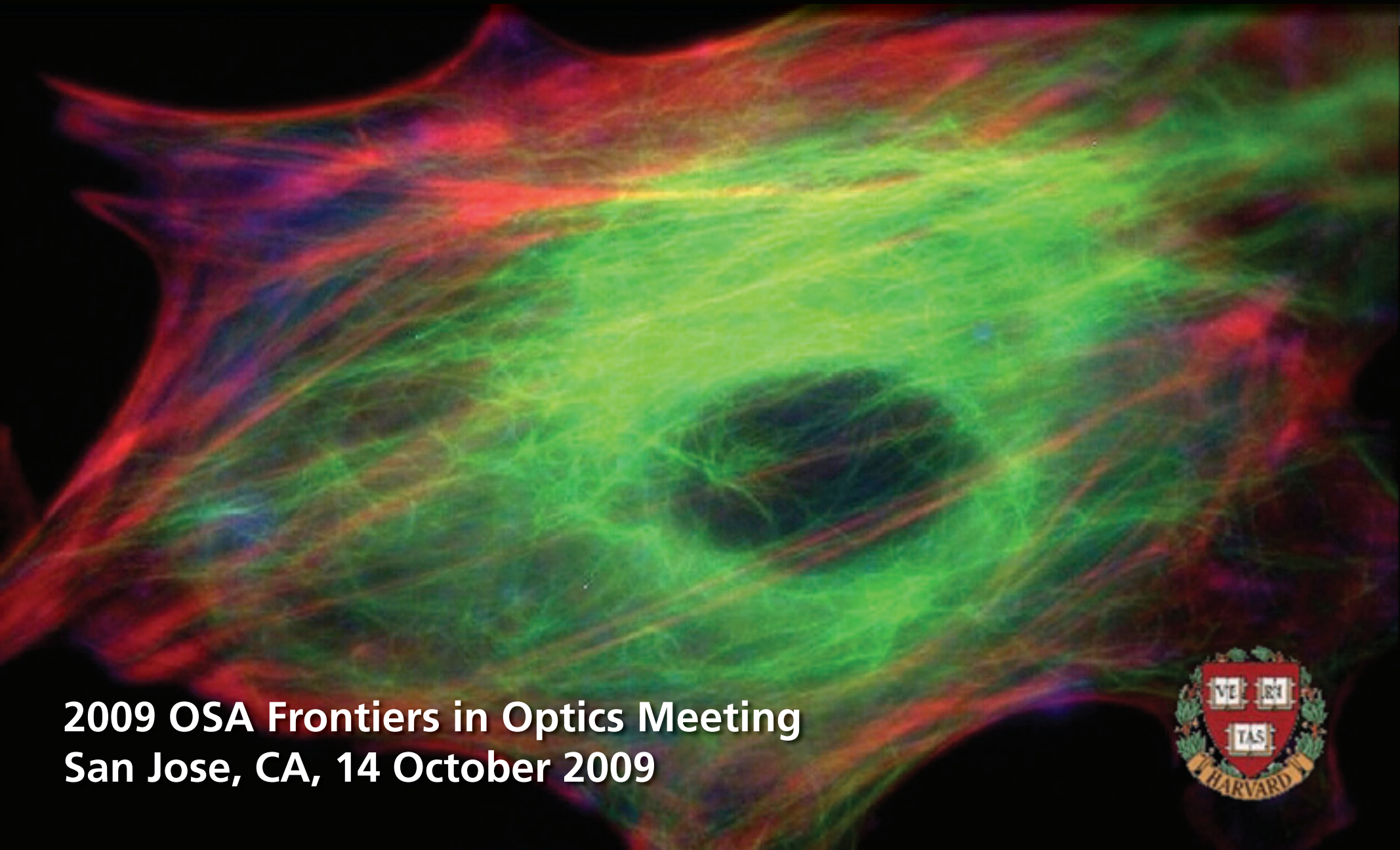
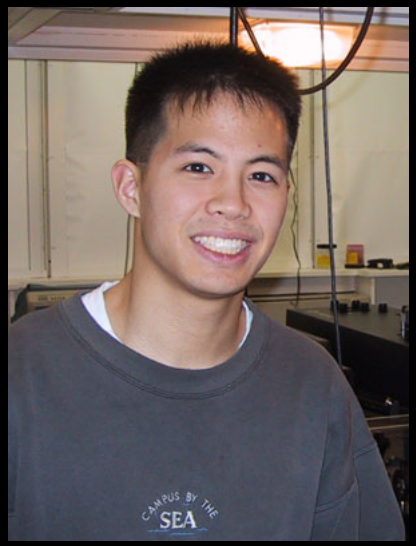
Nanosurgery with femtosecond lasers



2009 OSA Frontiers in Optics Meeting
San Jose, CA, 14 October 2009

Iva Maxwell



Sam Chung

Valeria Nuzzo

Alexander Heisterkamp

and also....

Dr. Eli Glezer
Prof. Chris Schaffer
Nozomi Nishimura
Debayoti Datta
Dr. Jonathan Ashcom
Jeremy Hwang
Dr. Nan Shen
Roanna Ruiz
Anja Schmalz
Prakriti Tayalia

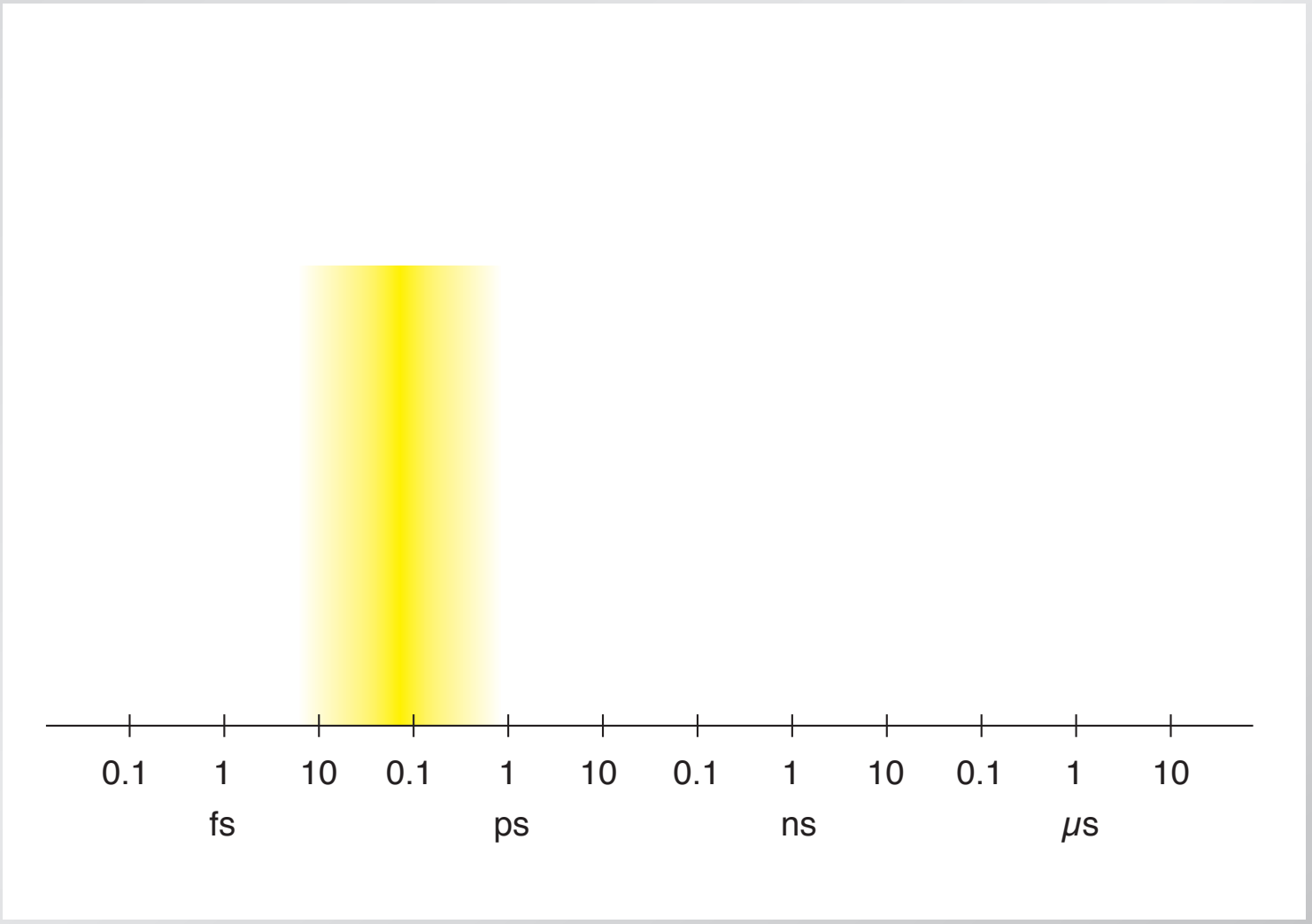
Prof. Don Ingber (Harvard Medical School)
Prof. Aravi Samuel (Harvard)
Prof. Chris Gabel (Boston University)
Dr. Damon Clark (Harvard University)
Prof. J.M. Underwood (UMass Worcester)
Prof. J.A. Nickerson (UMass Worcester)
Prof. Philip LeDuc (Carnegie Mellon)
Prof. Sanjay Kumar (UC Berkeley)

Introduction

why use femtosecond pulses?

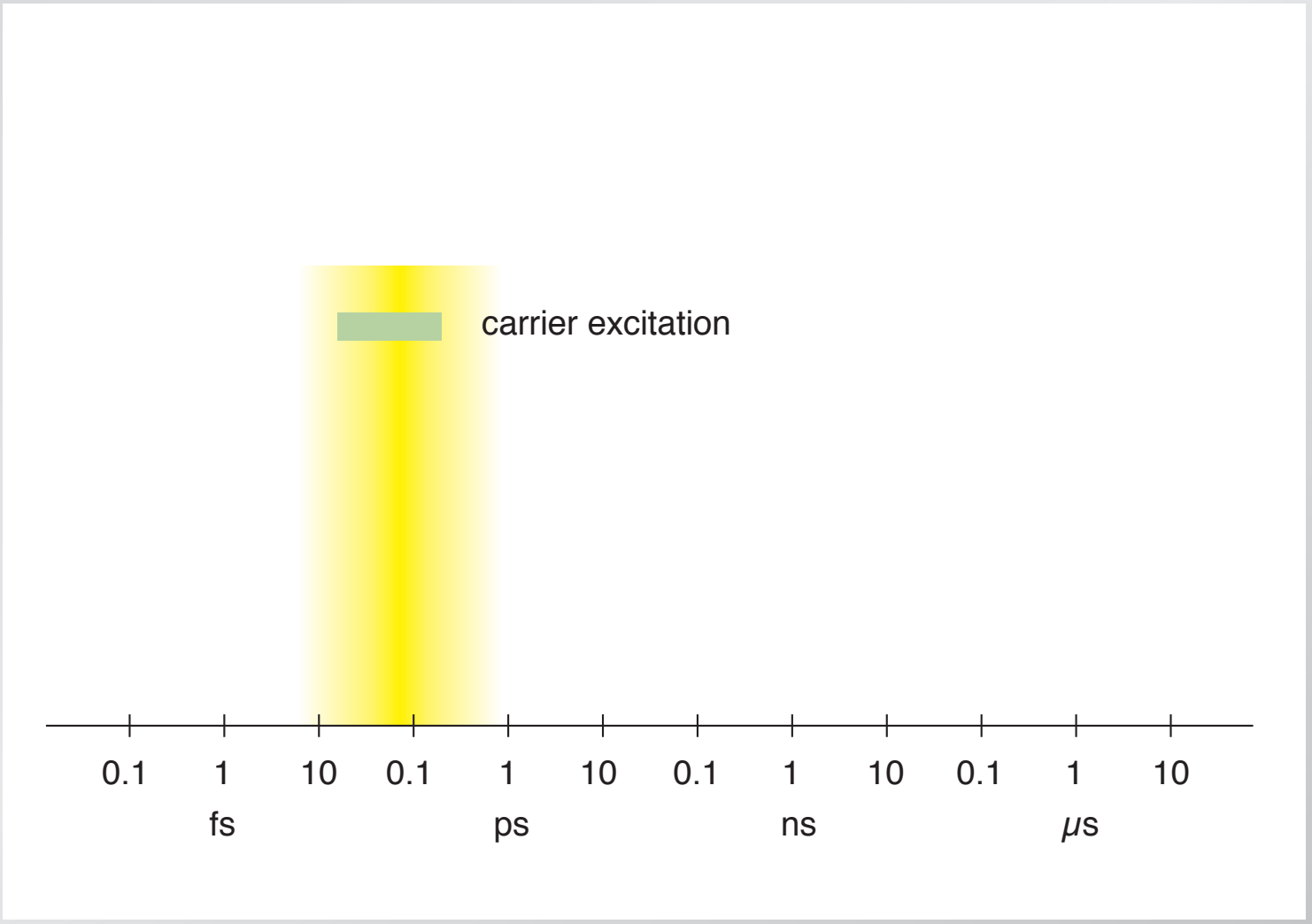
Introduction

relevant time scales



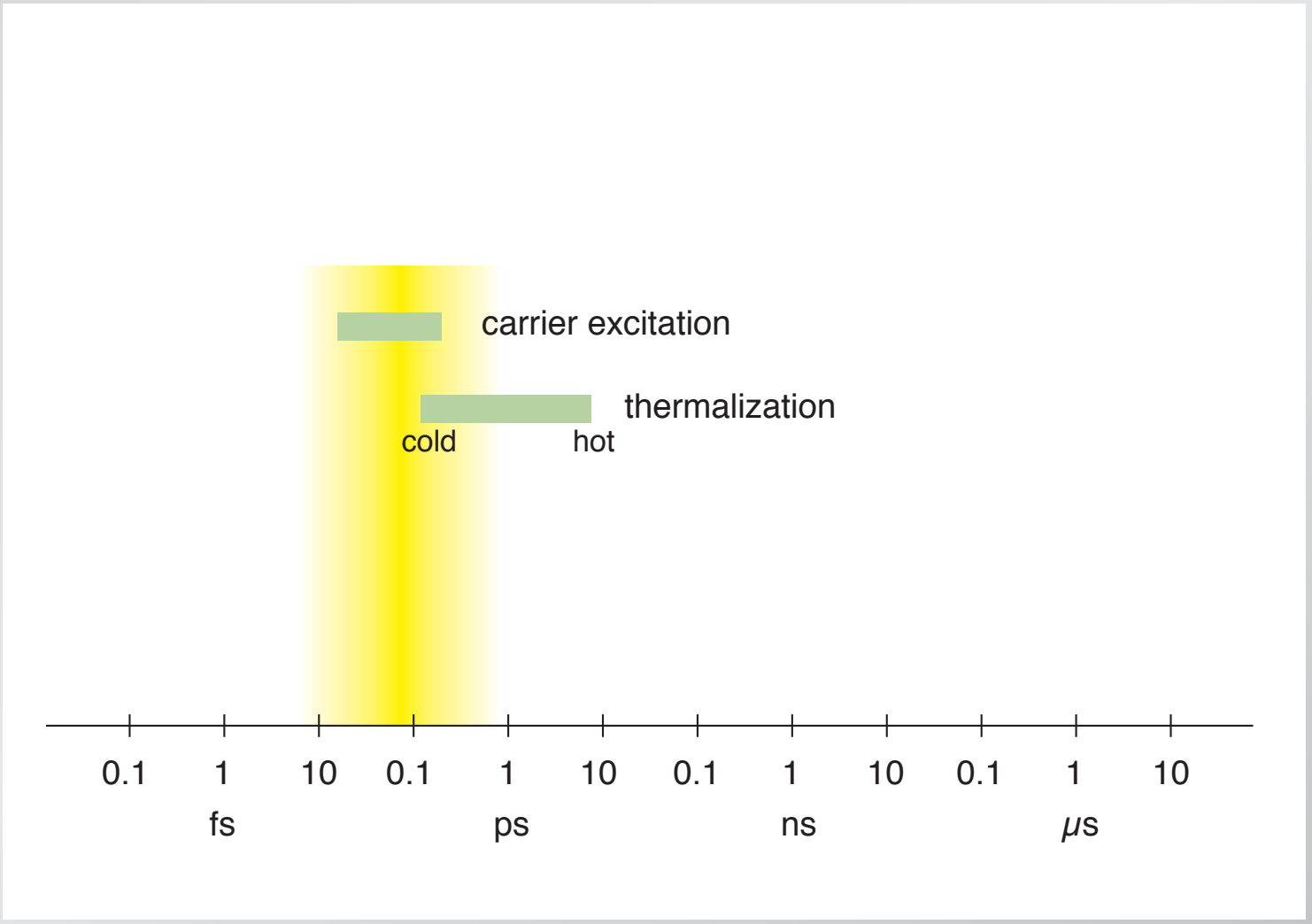
Introduction

relevant time scales



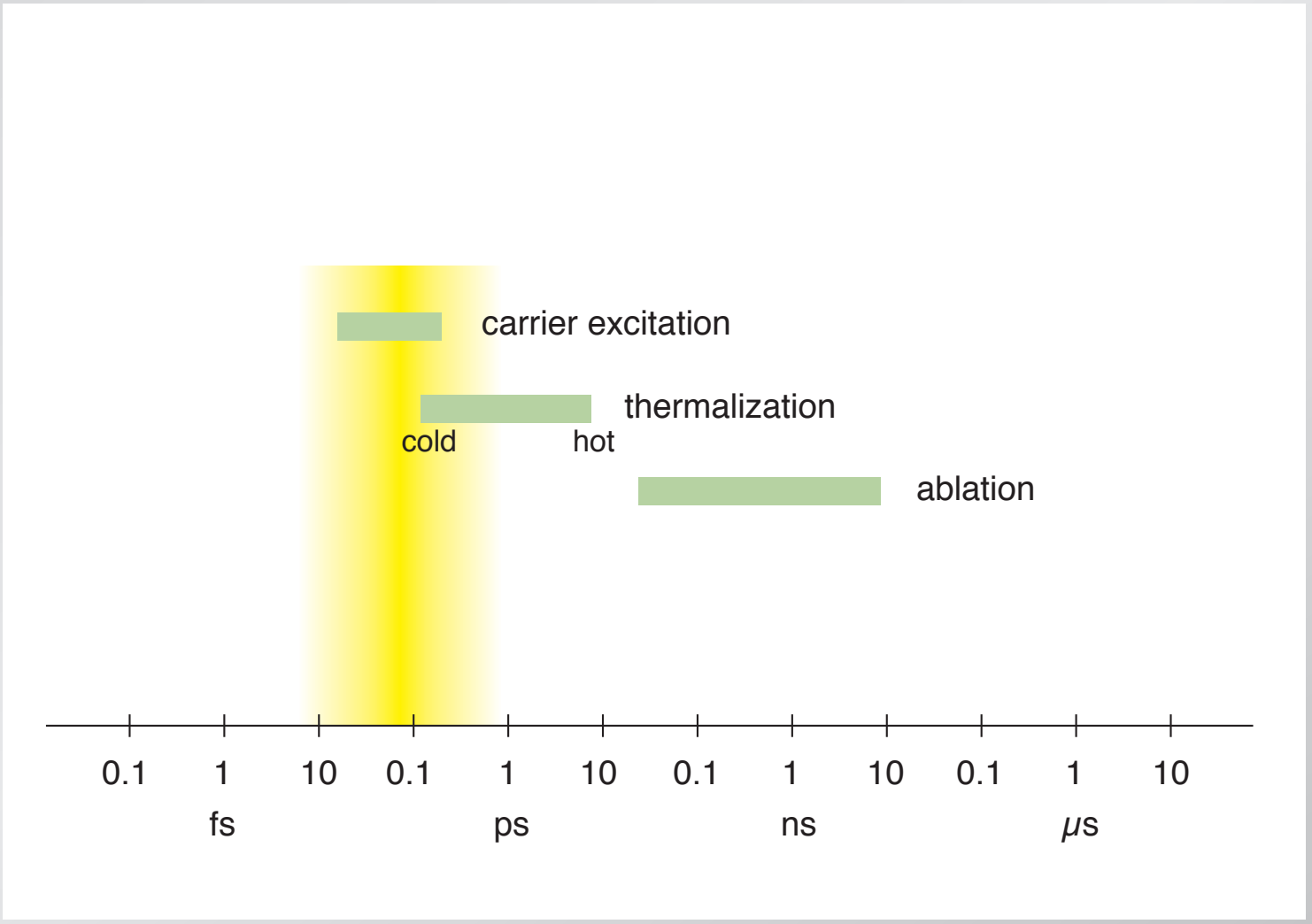
Introduction

relevant time scales



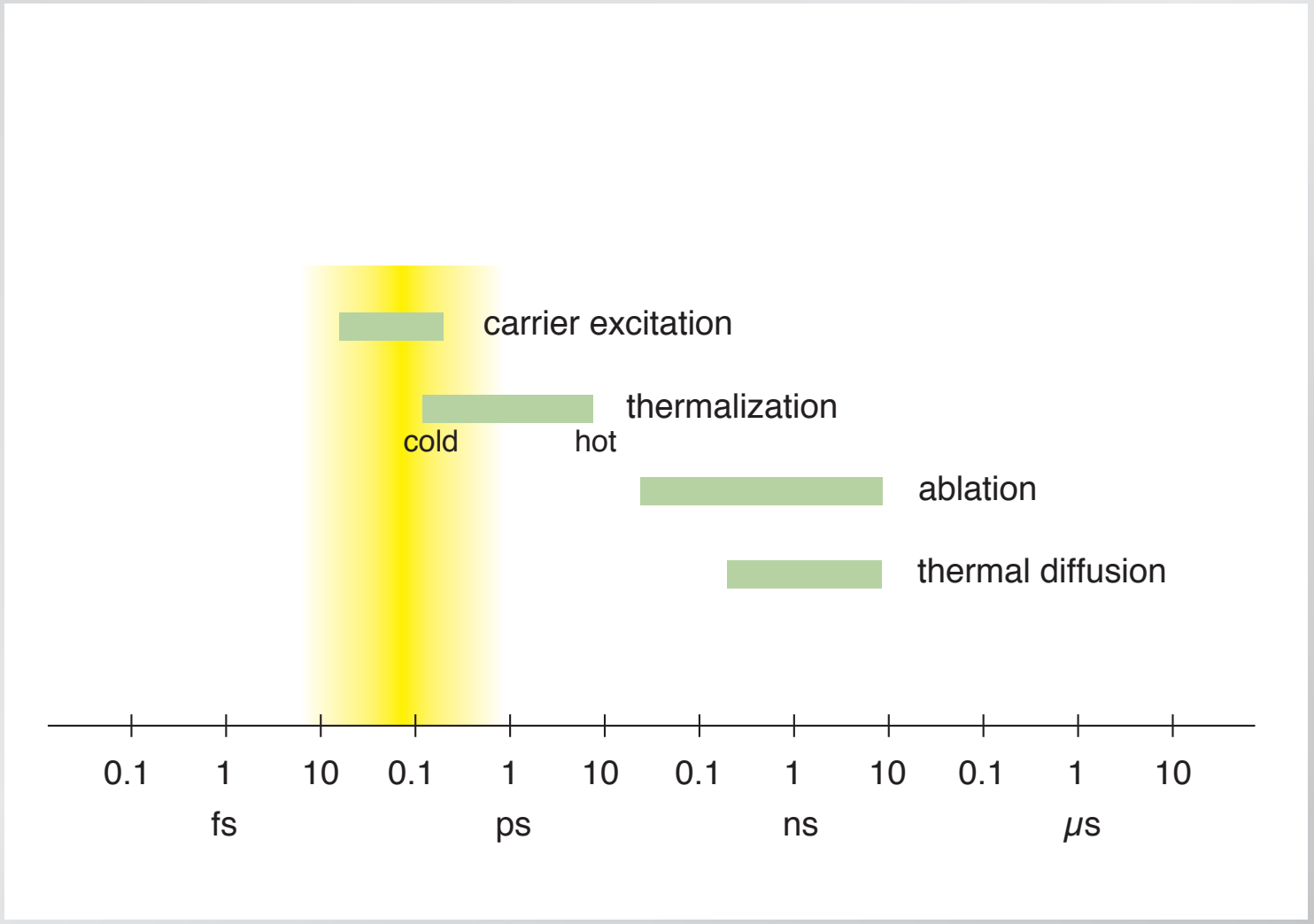
Introduction

relevant time scales



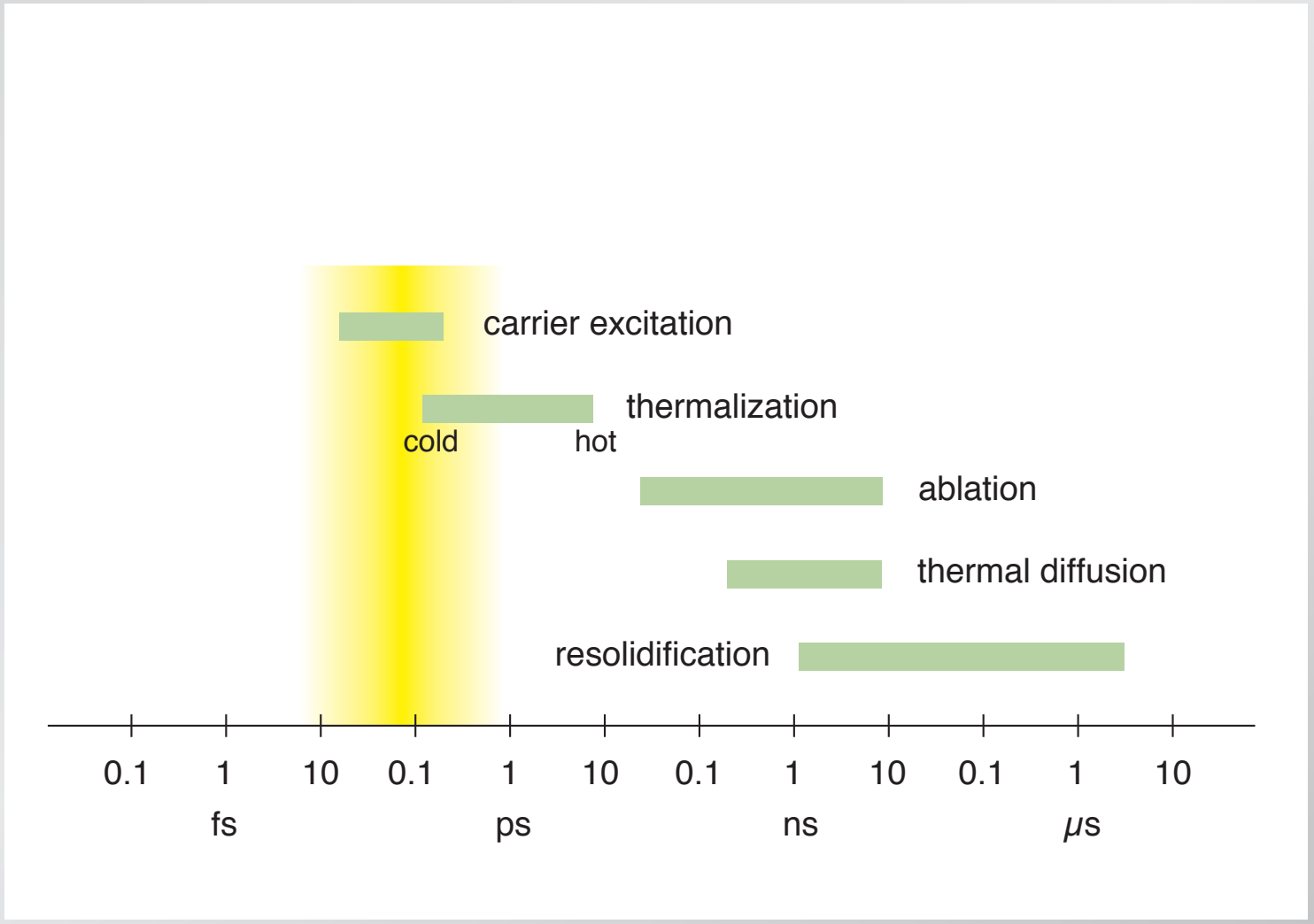
Introduction

relevant time scales



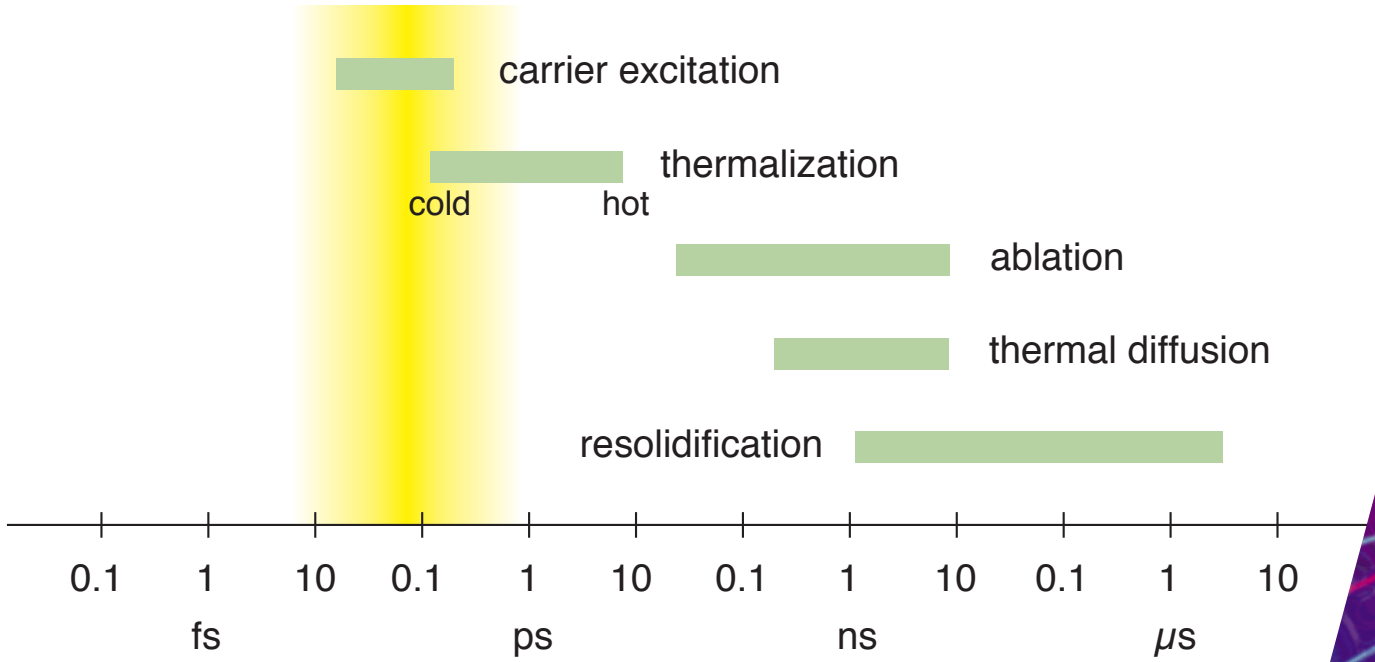
Introduction

relevant time scales



Introduction

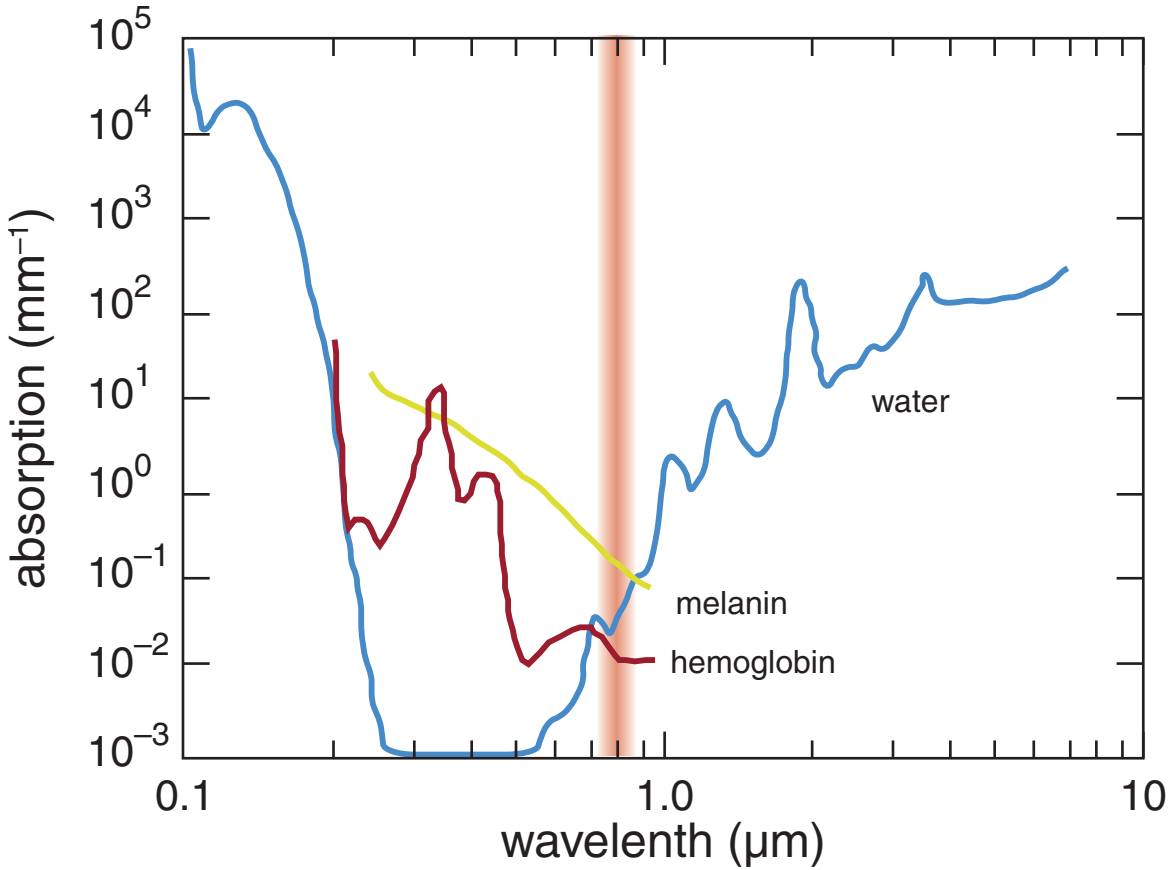
relevant time scales



Nature Materials **1**, 217 (2002)

Introduction

tissue is nearly transparent at 800 nm

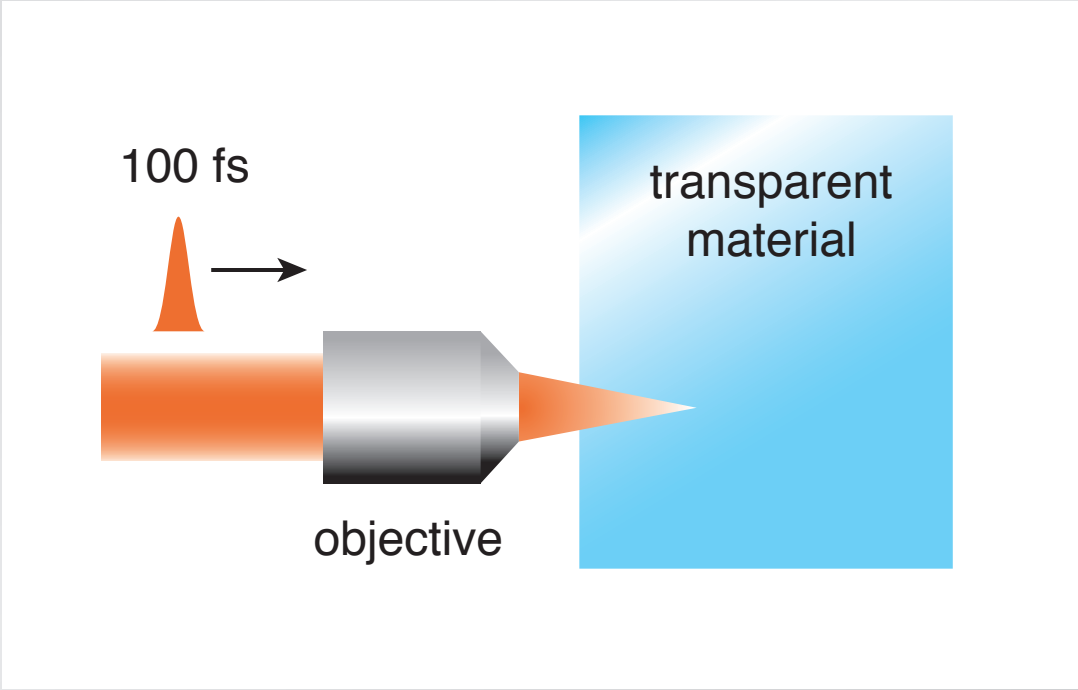


Outline

- femtosecond materials interactions
- subcellular surgery
- nanoneurosurgery

Femtosecond materials interactions

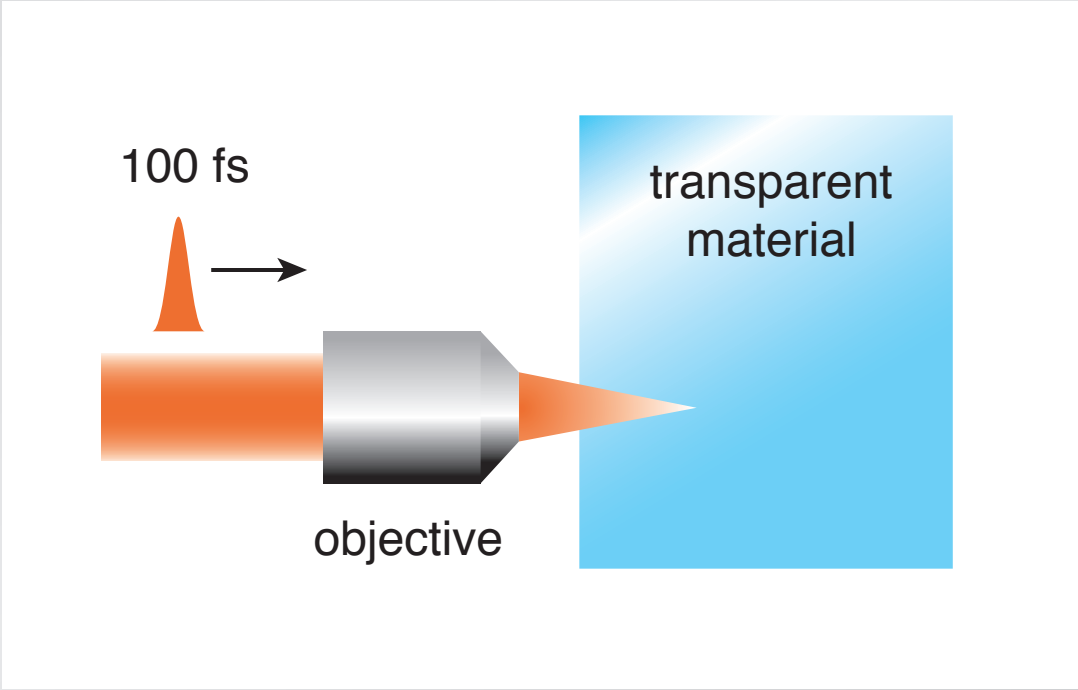
focus laser beam inside material



Opt. Lett. **21**, 2023 (1996)

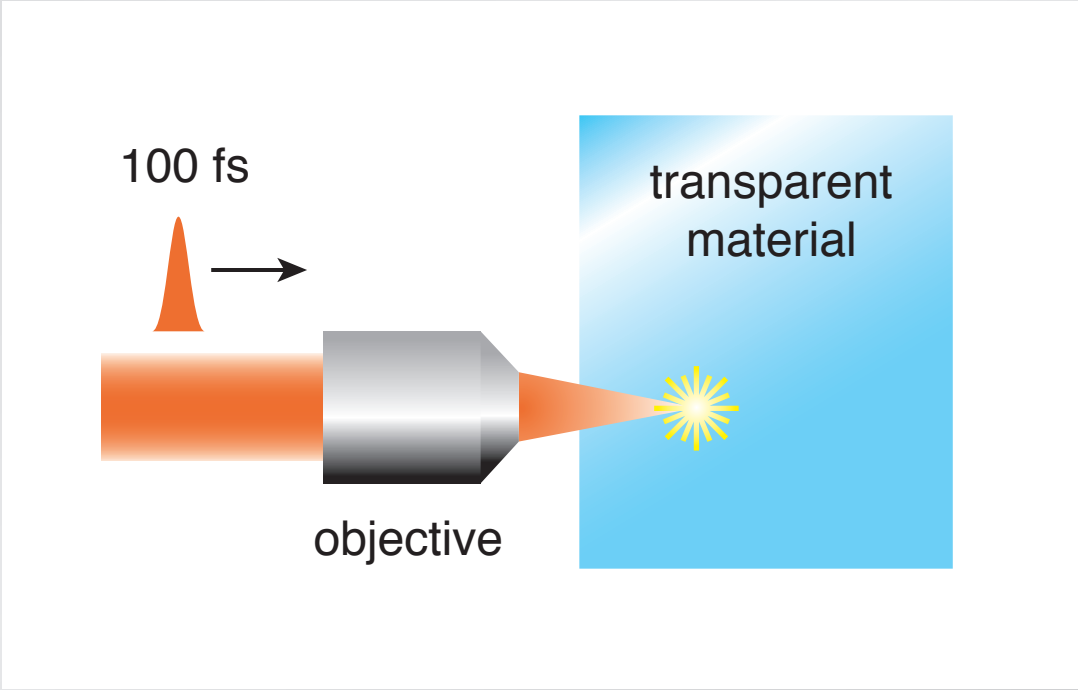
Femtosecond materials interactions

high intensity at focus…



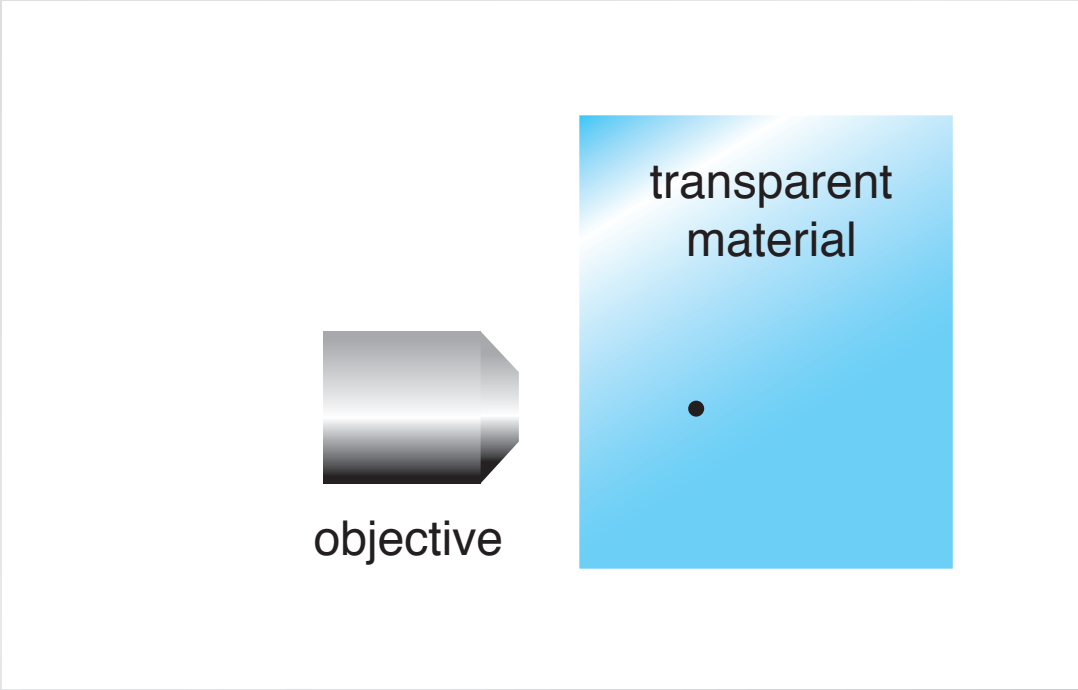
Femtosecond materials interactions

…causes nonlinear ionization…

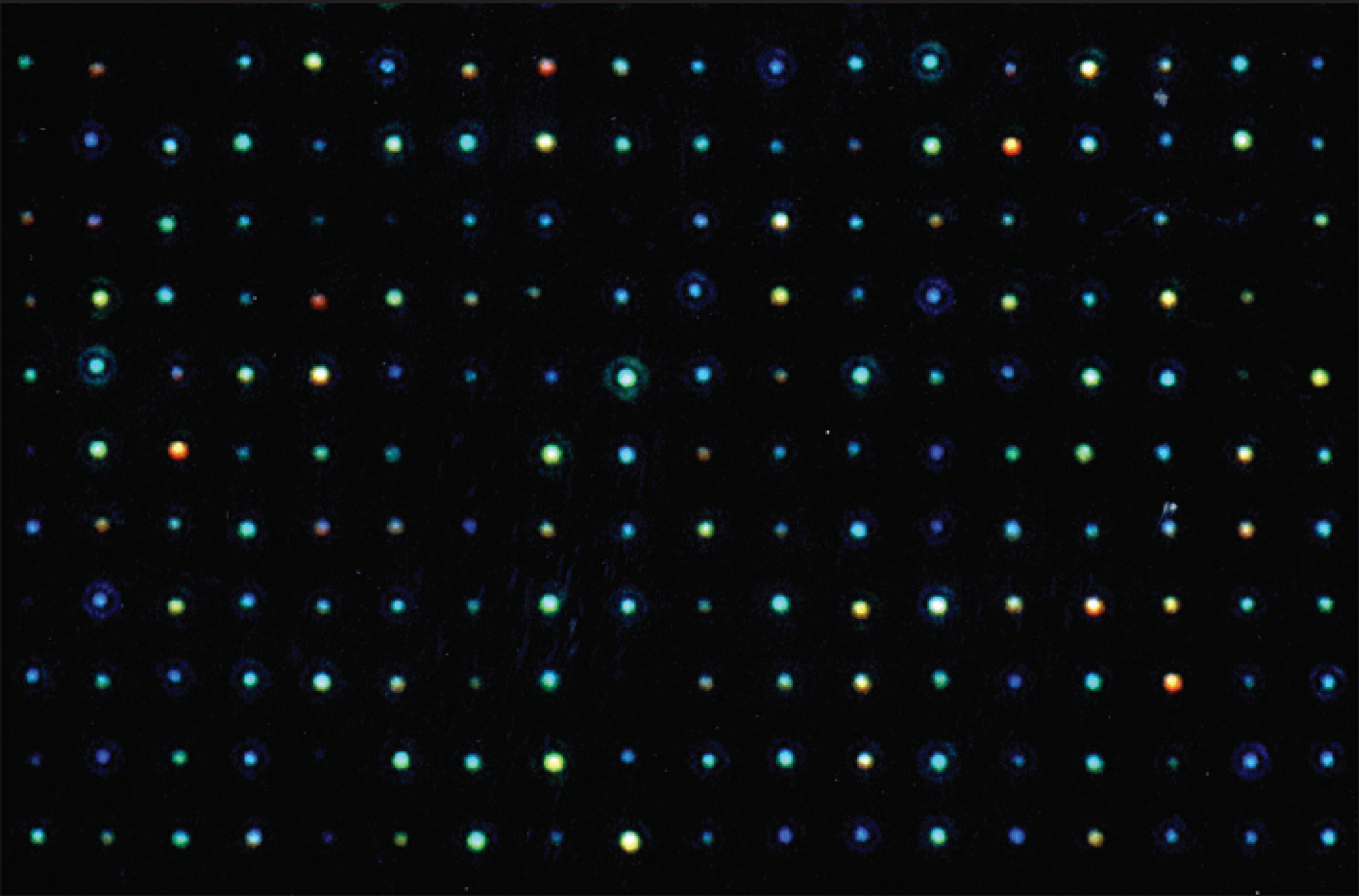


Femtosecond materials interactions

and ‘microexplosion’ causes microscopic damage…



Femtosecond materials interactions

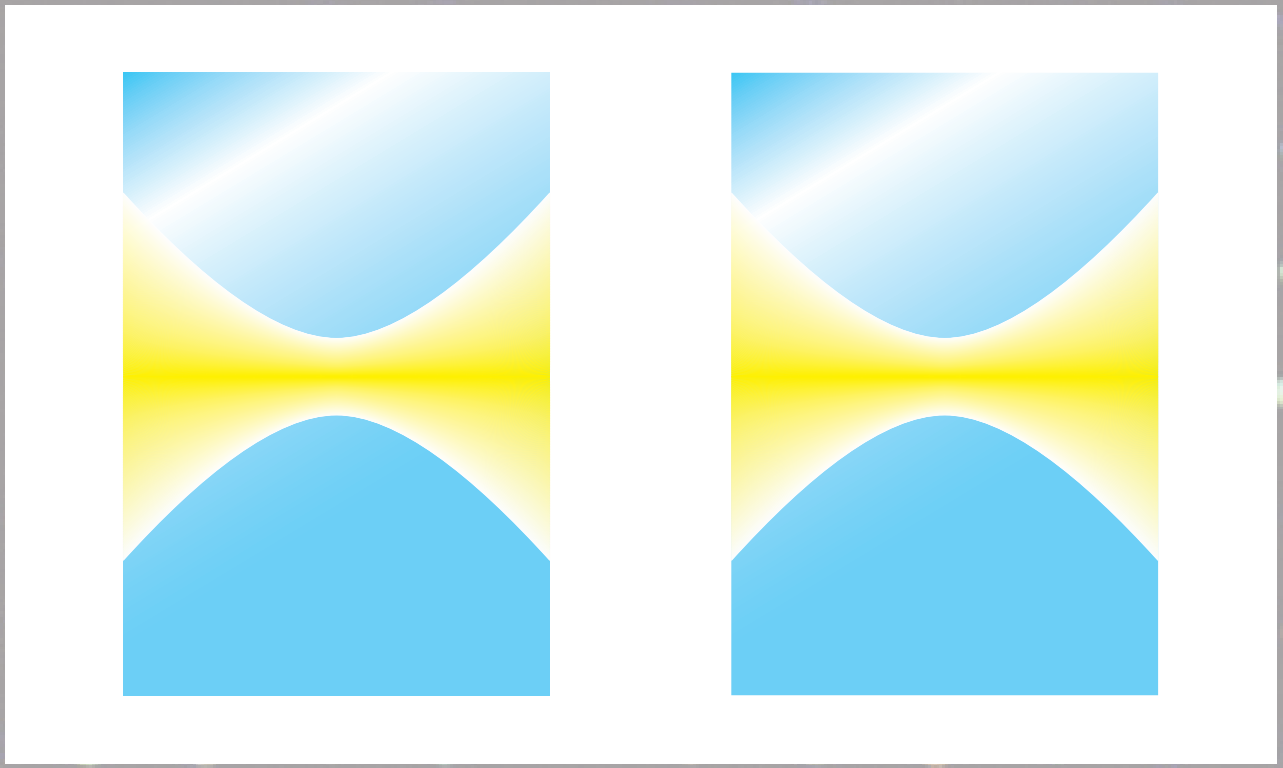


Femtosecond materials interactions

photon energy < bandgap $\longrightarrow$ nonlinear interaction

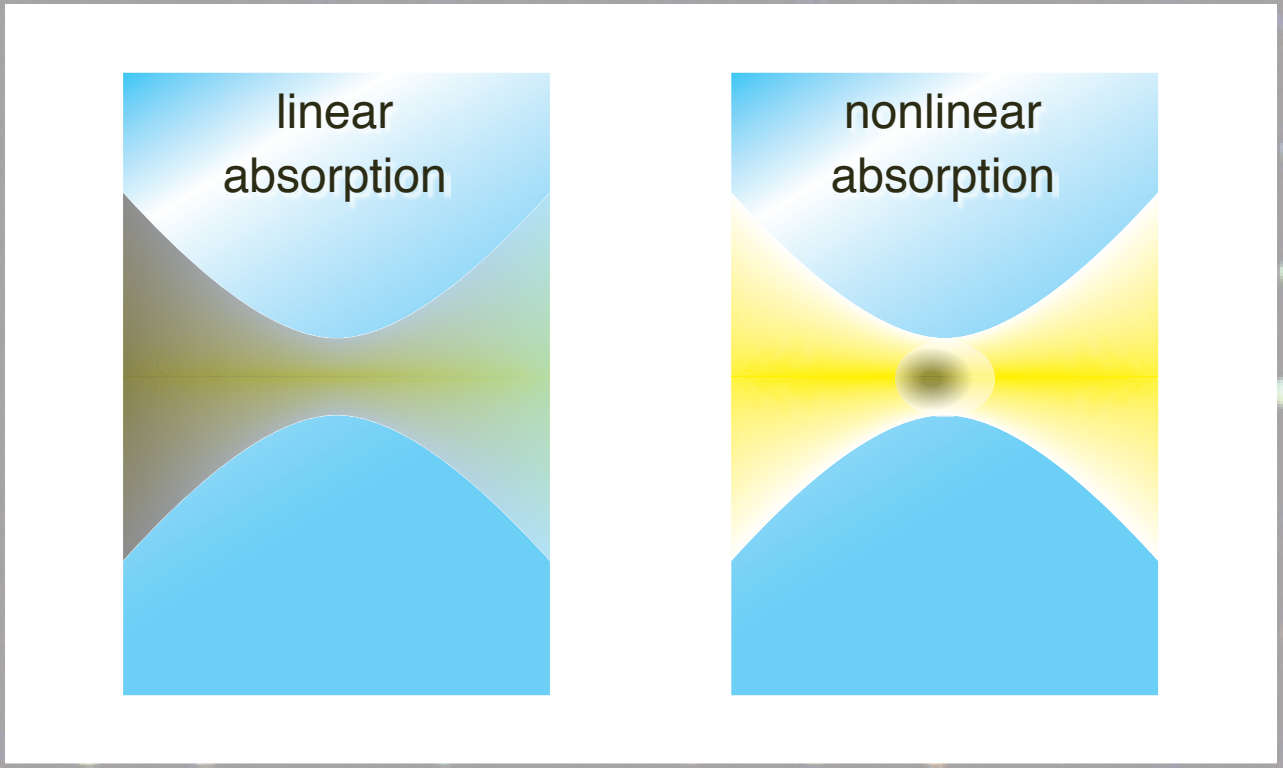
Femtosecond materials interactions

nonlinear interaction provides bulk confinement

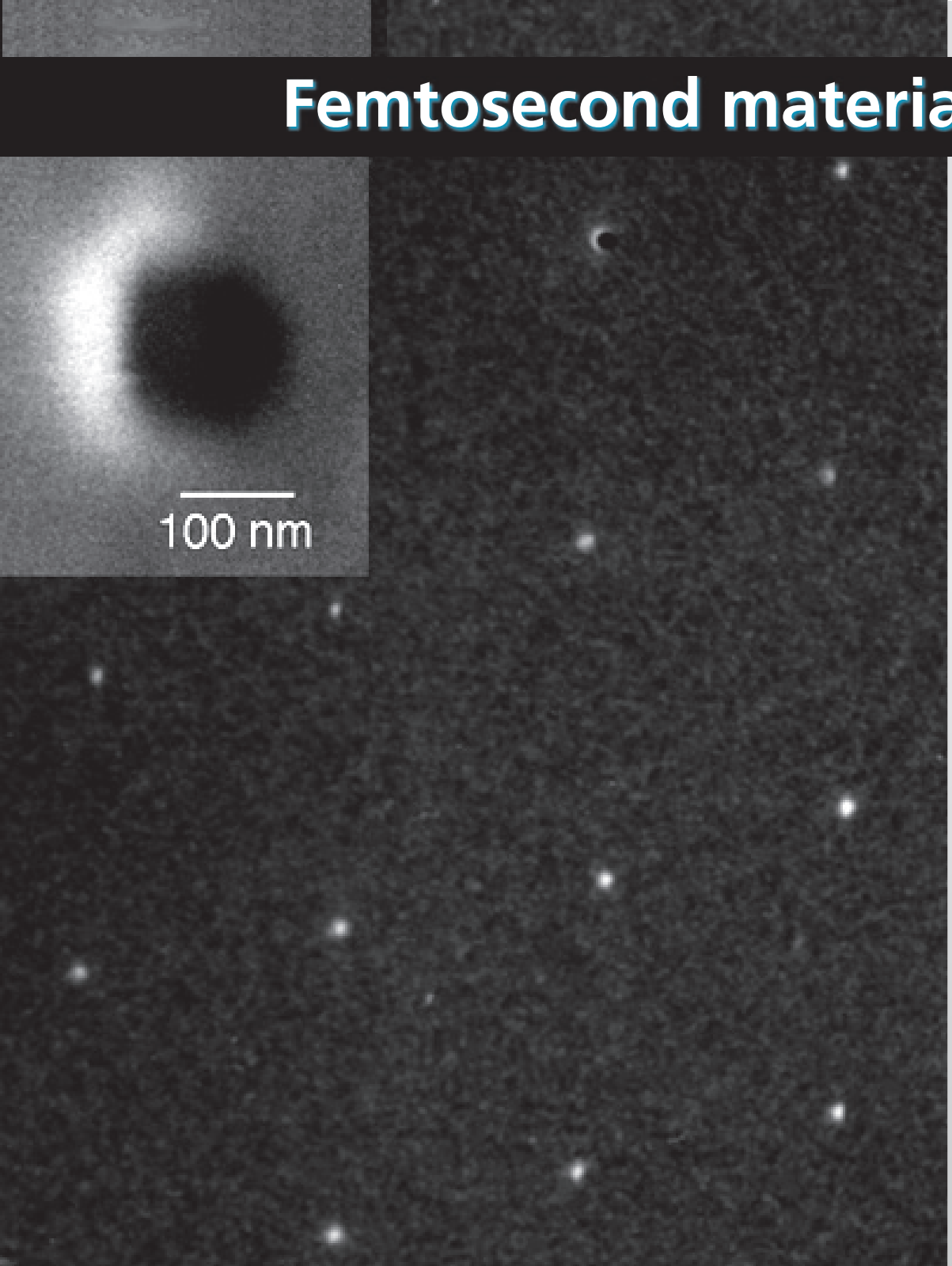


Femtosecond materials interactions

nonlinear interaction provides bulk confinement



Femtosecond materials interactions

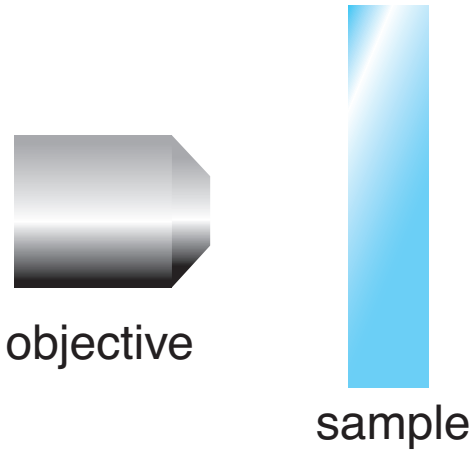


SEM & AFM:

- **100-nm cavities**
- **little colateral damage**

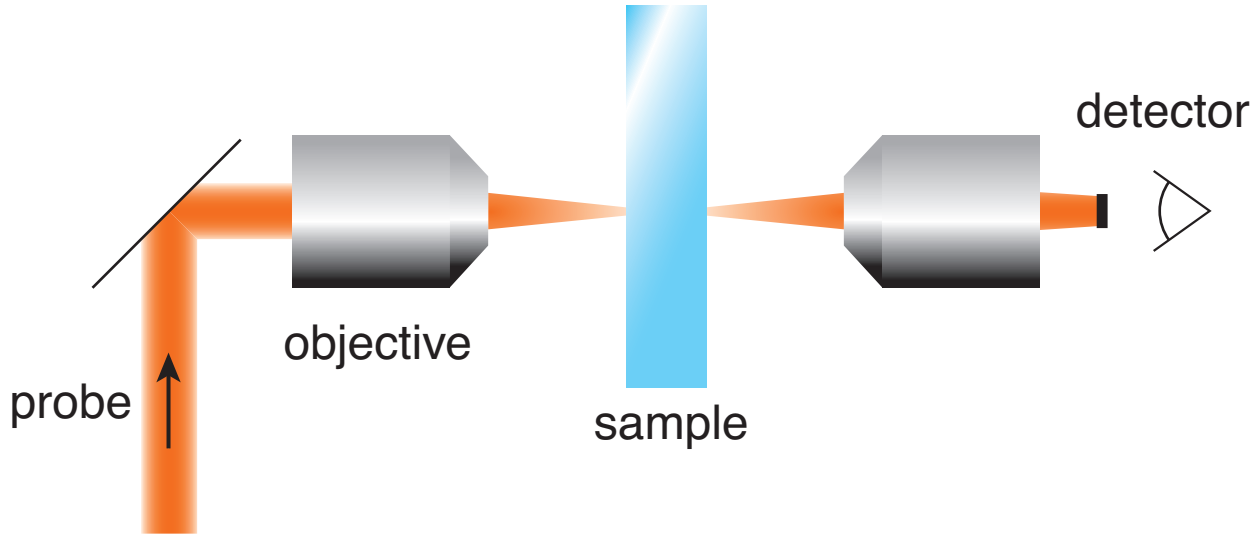
Femtosecond materials interactions

Dark-field scattering



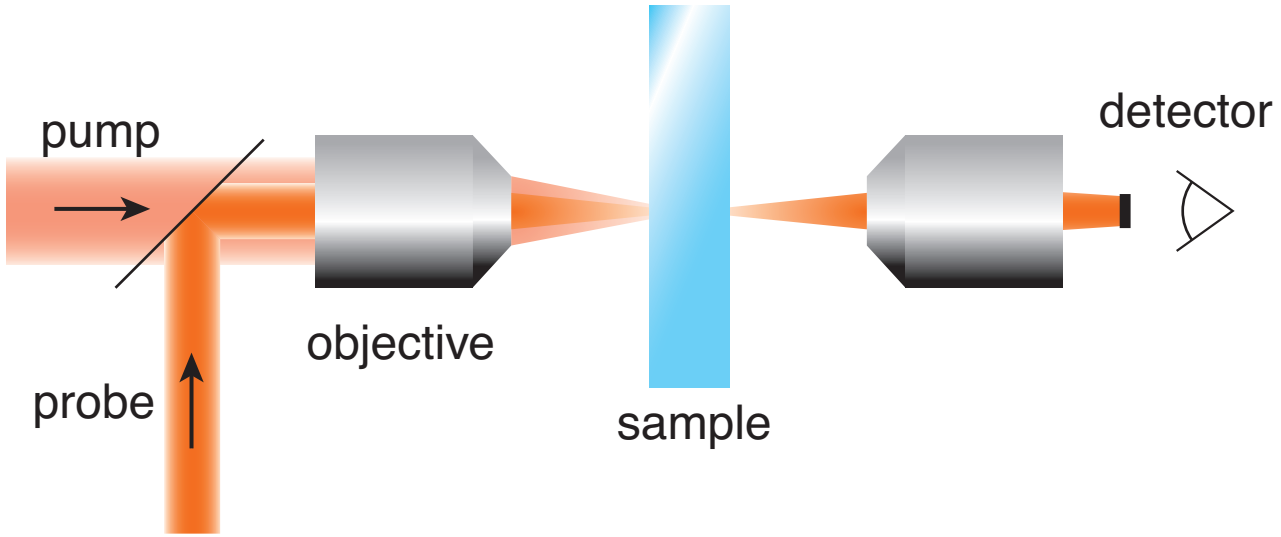
Femtosecond materials interactions

block probe beam…



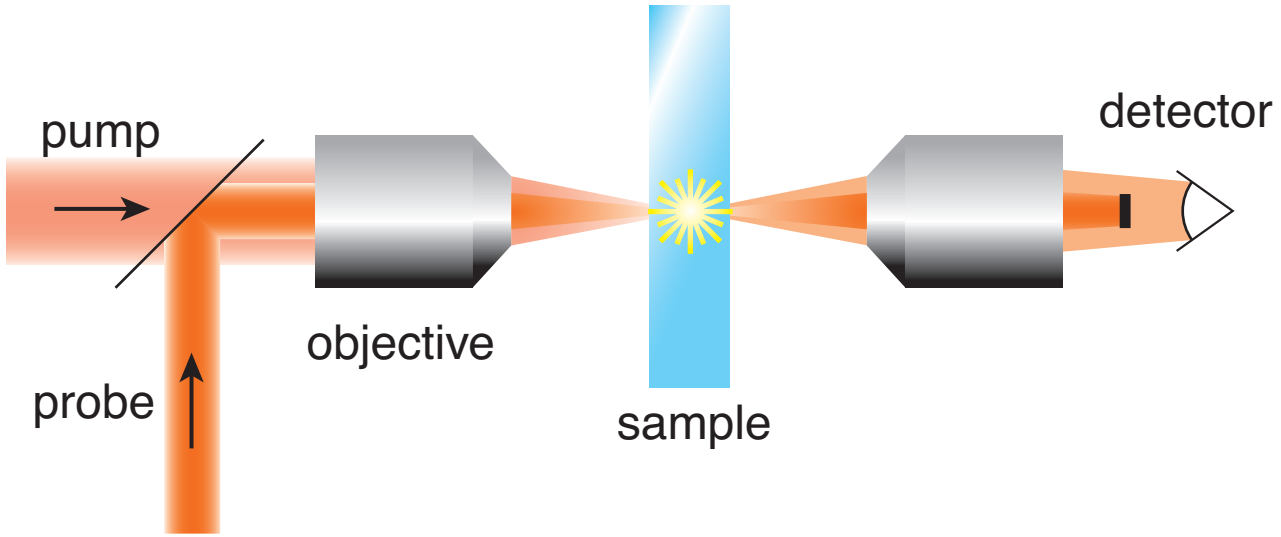
Femtosecond materials interactions

… bring in pump beam…



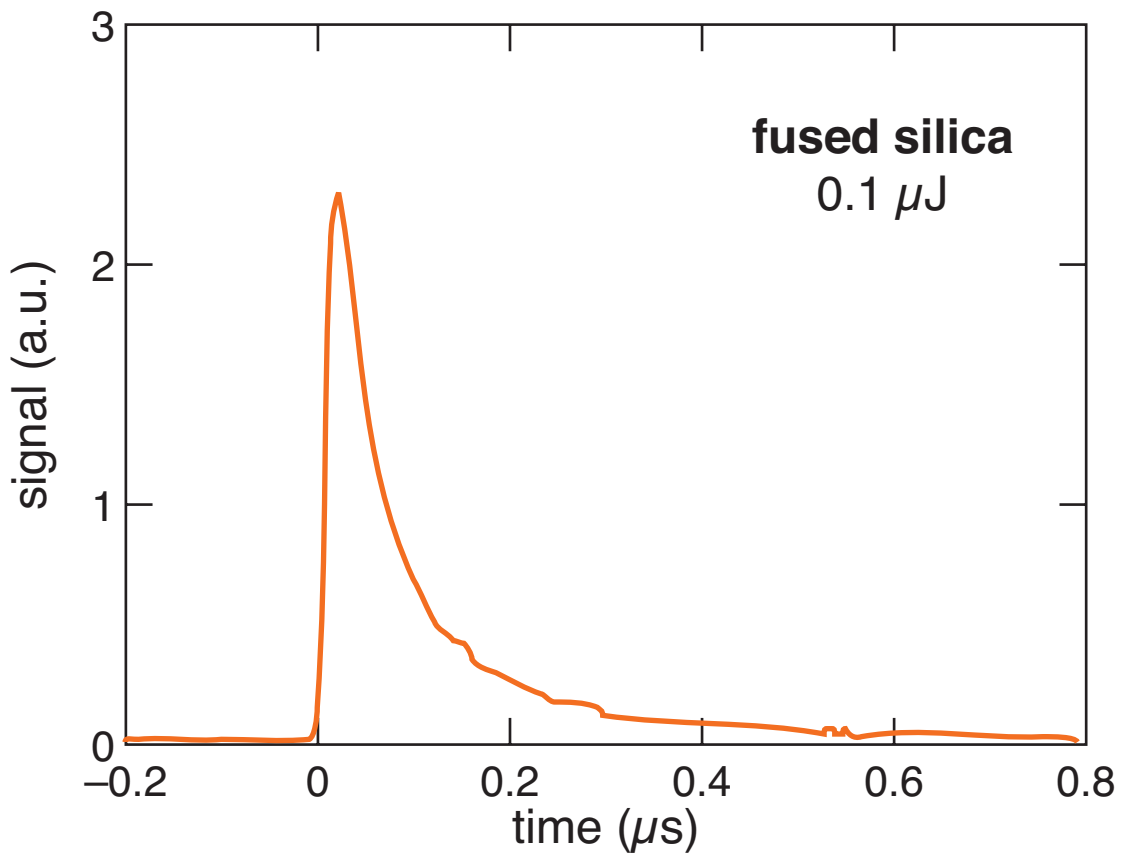
Femtosecond materials interactions

… damage scatters probe beam



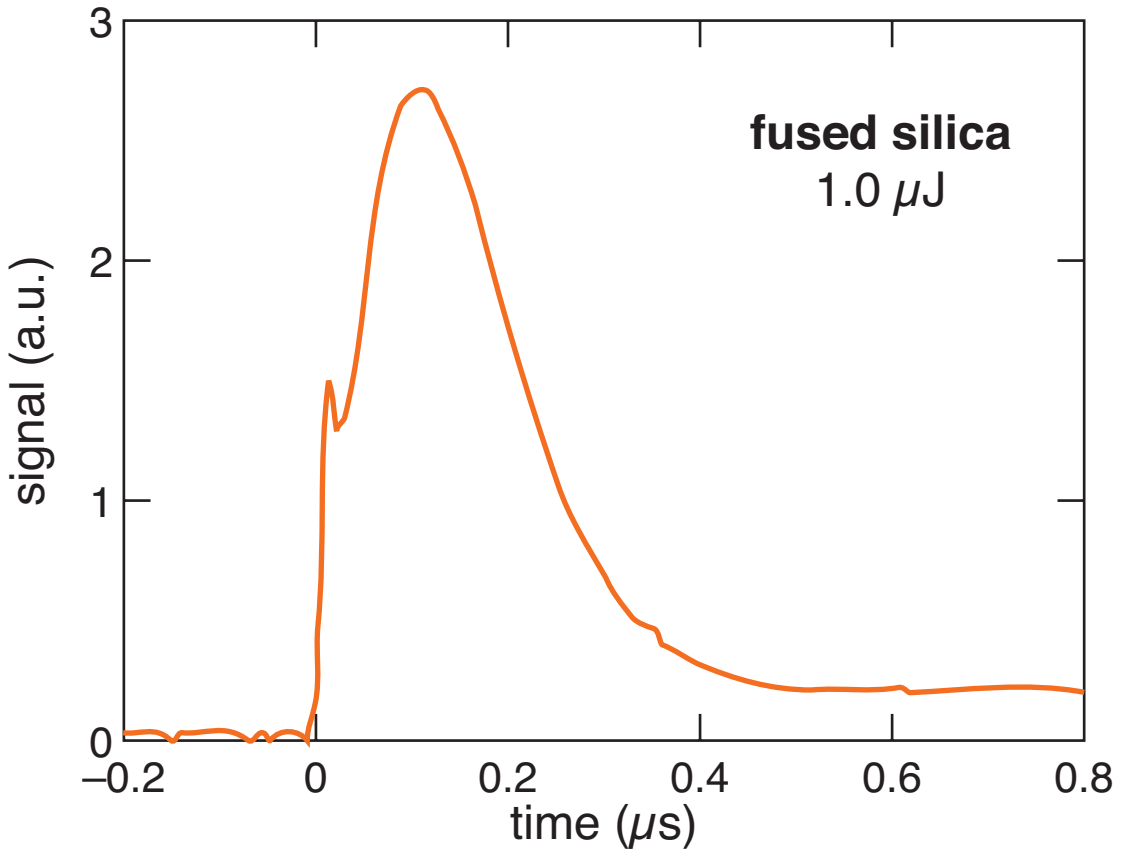
Femtosecond materials interactions

scattered signal



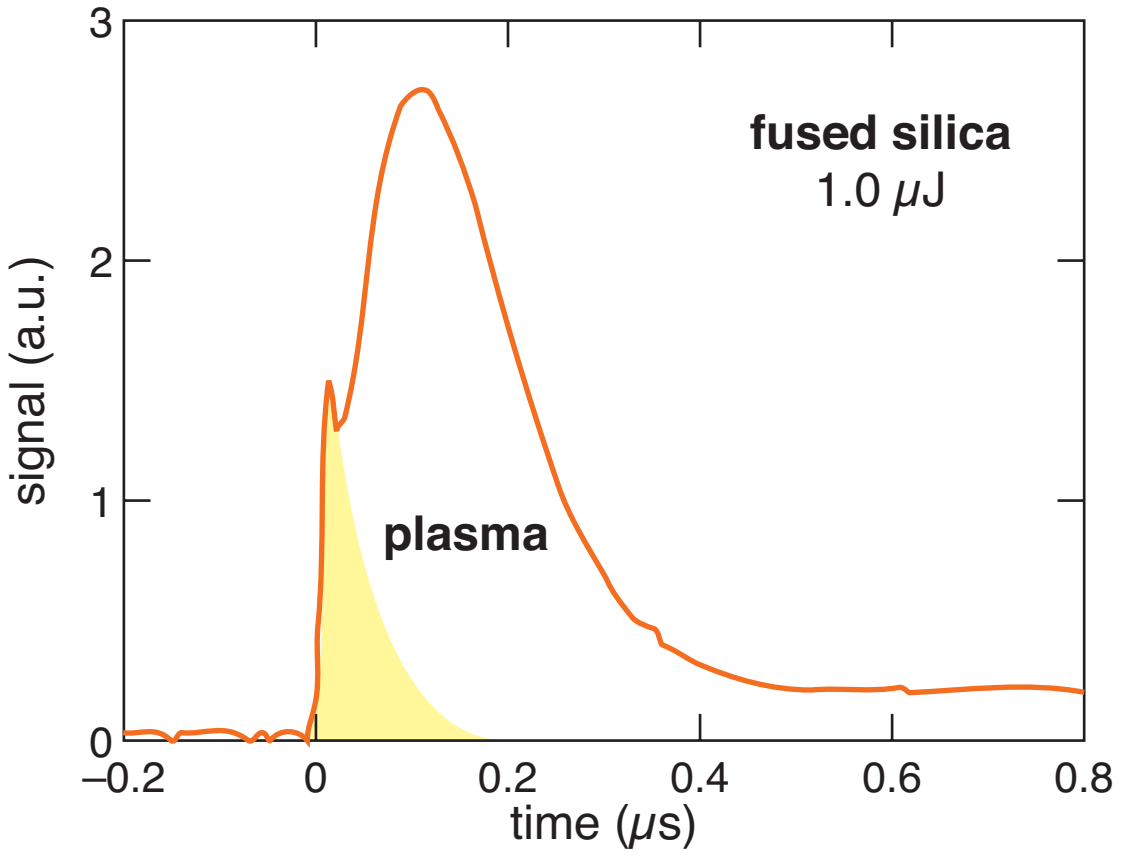
Femtosecond materials interactions

scattered signal



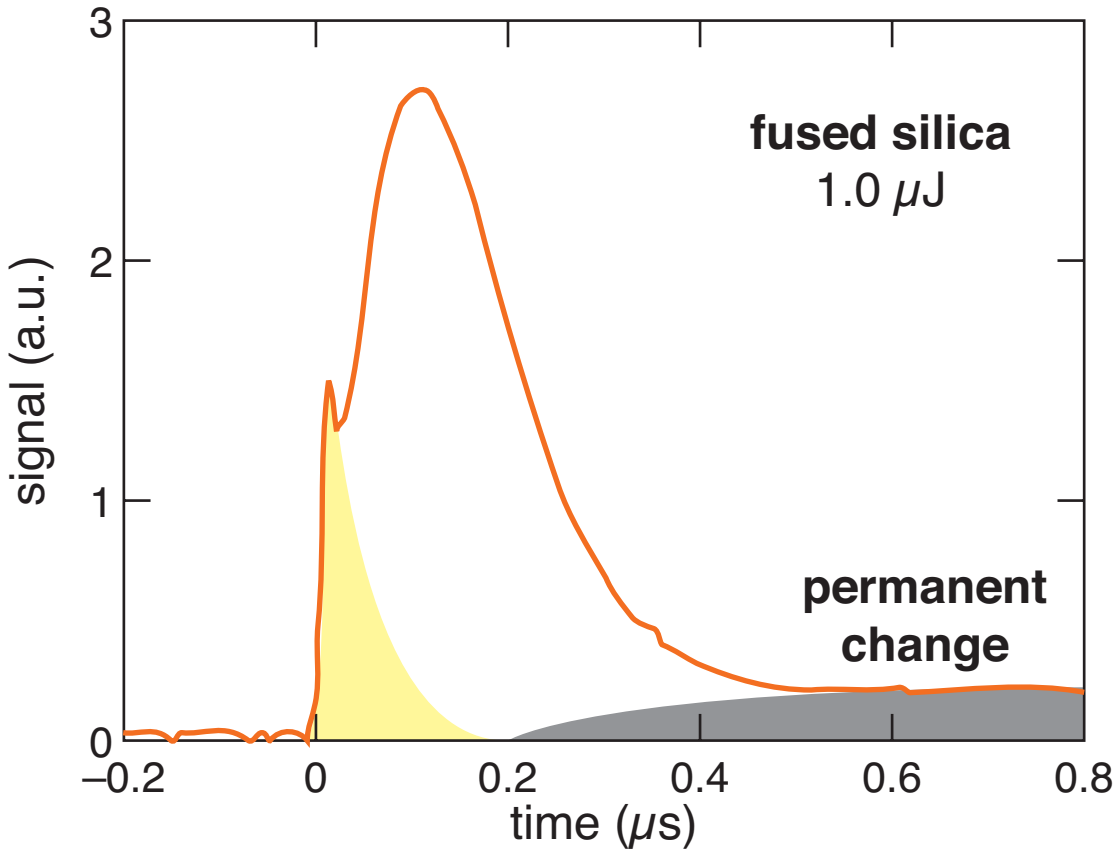
Femtosecond materials interactions

scattered signal



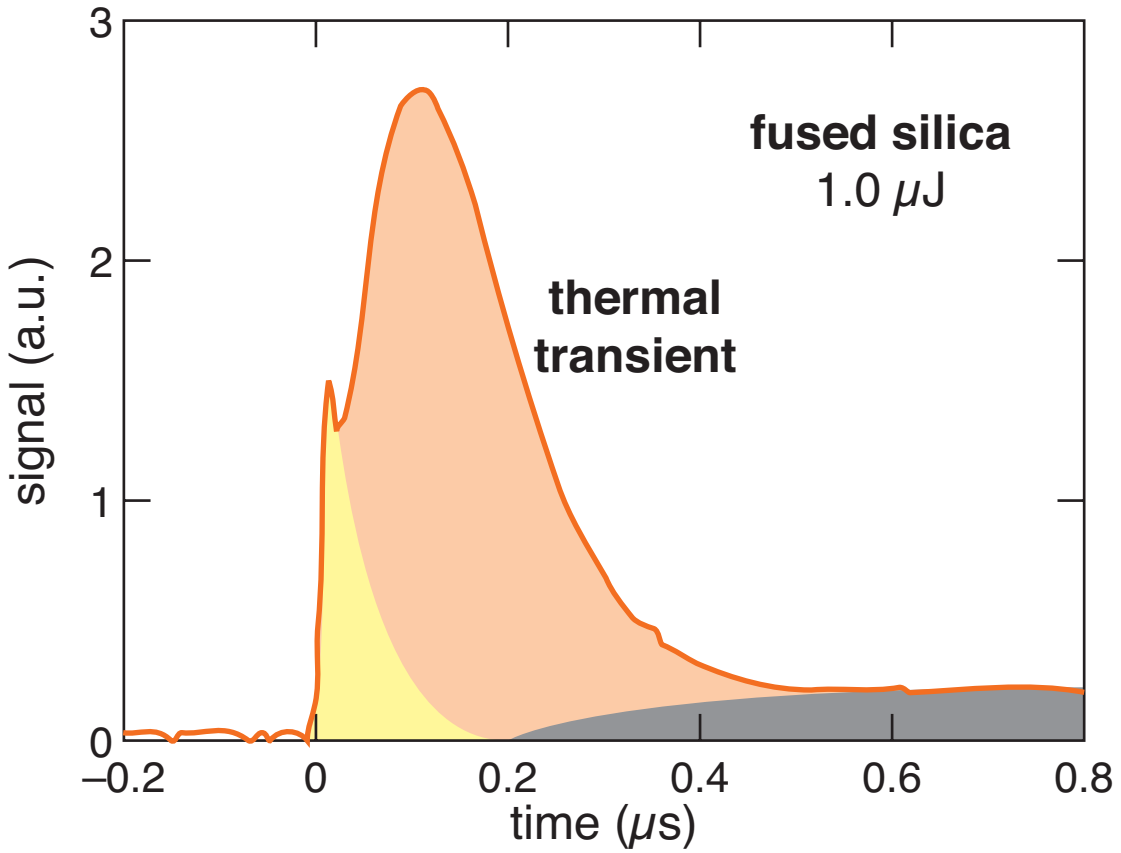
Femtosecond materials interactions

scattered signal



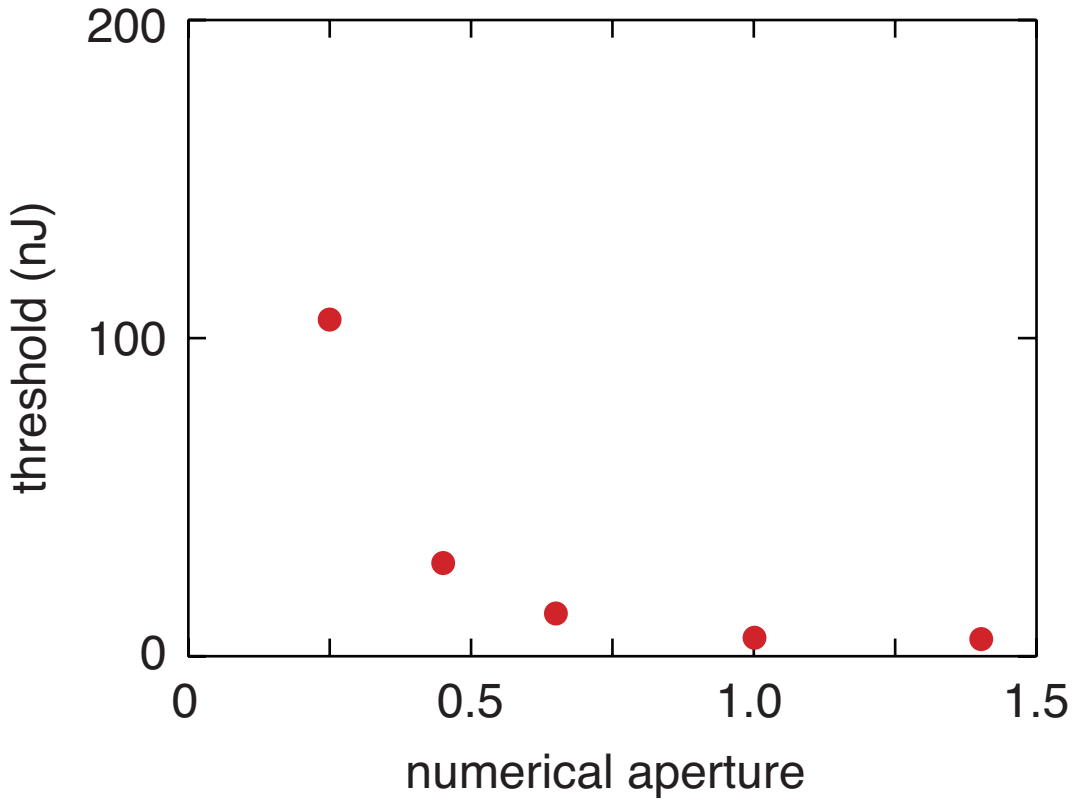
Femtosecond materials interactions

scattered signal



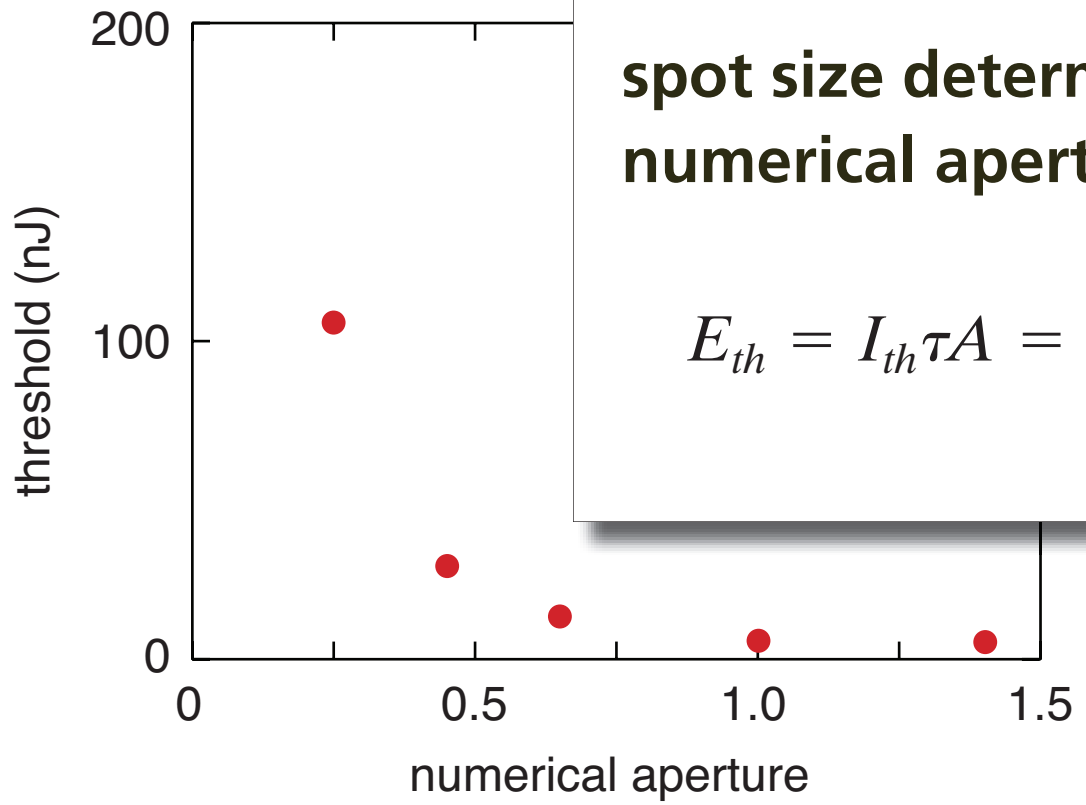
Femtosecond materials interactions

vary numerical aperture



Femtosecond materials interactions

vary numeric



intensity threshold:

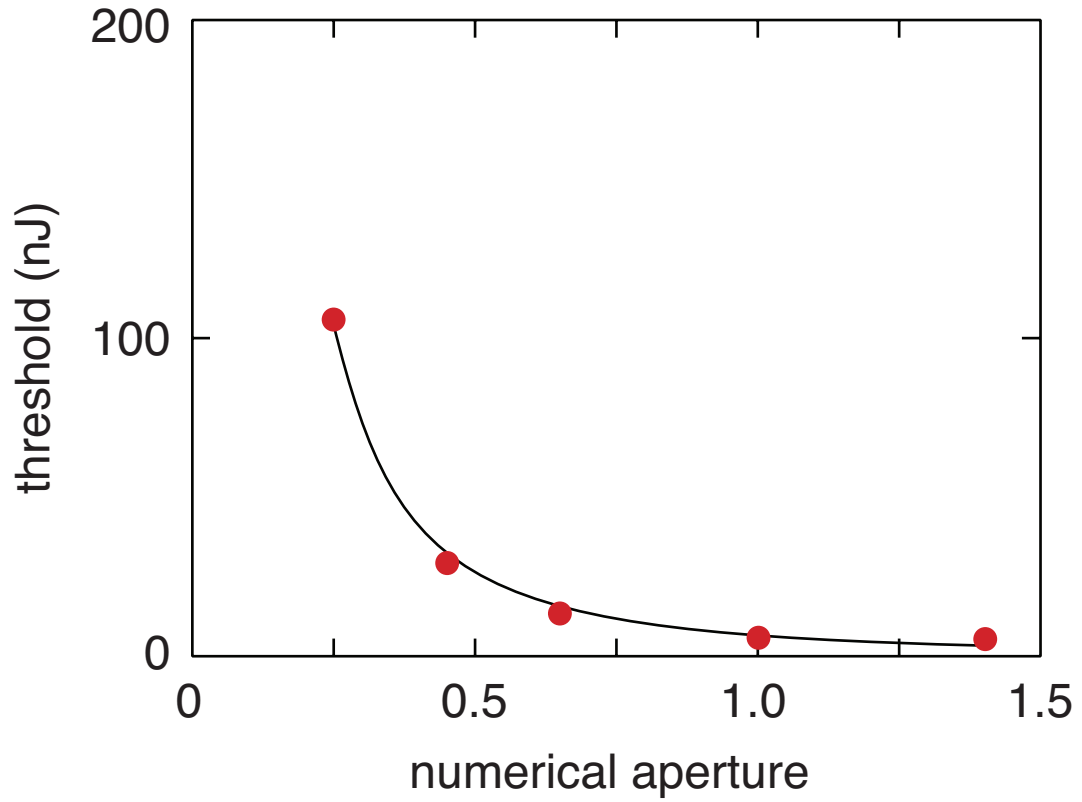
$$E_{th} = I_{th}\tau A$$

spot size determined by numerical aperture:

$$E_{th} = I_{th}\tau A = \frac{I_{th}\tau\lambda^2}{\pi(\mathrm{NA})^2}$$

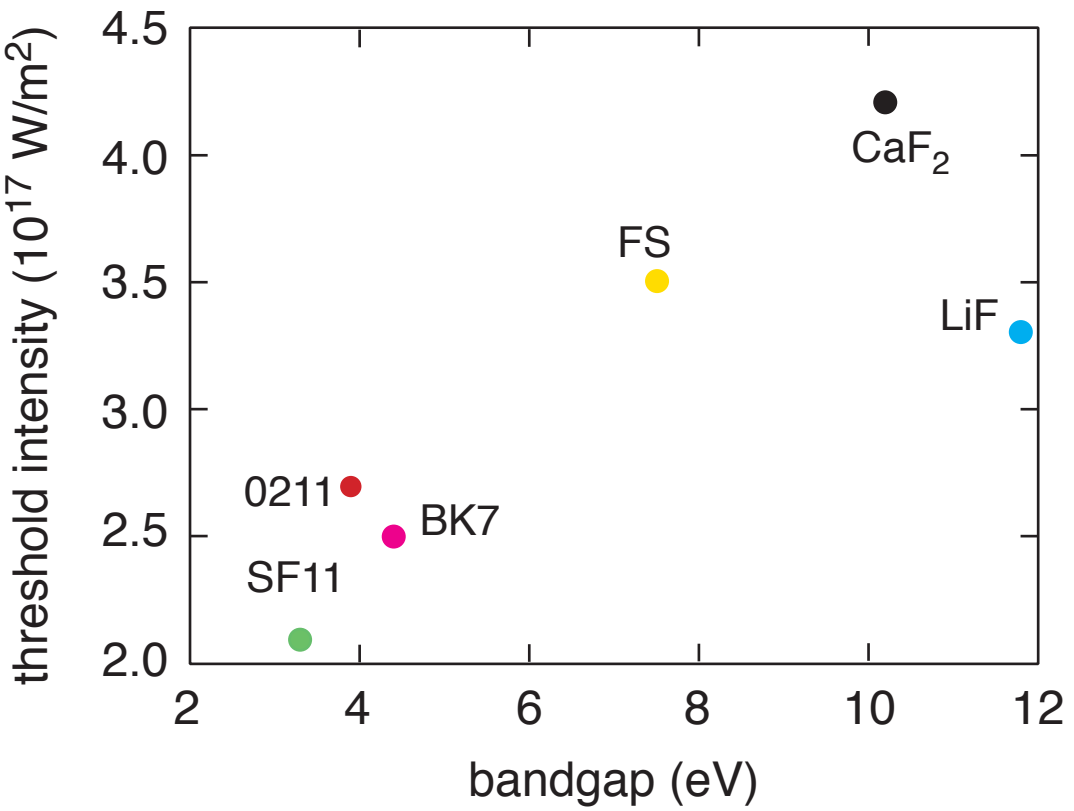
Femtosecond materials interactions

fit gives threshold intensity: I_{th} = 2.5 x 10^{17} W/m^2



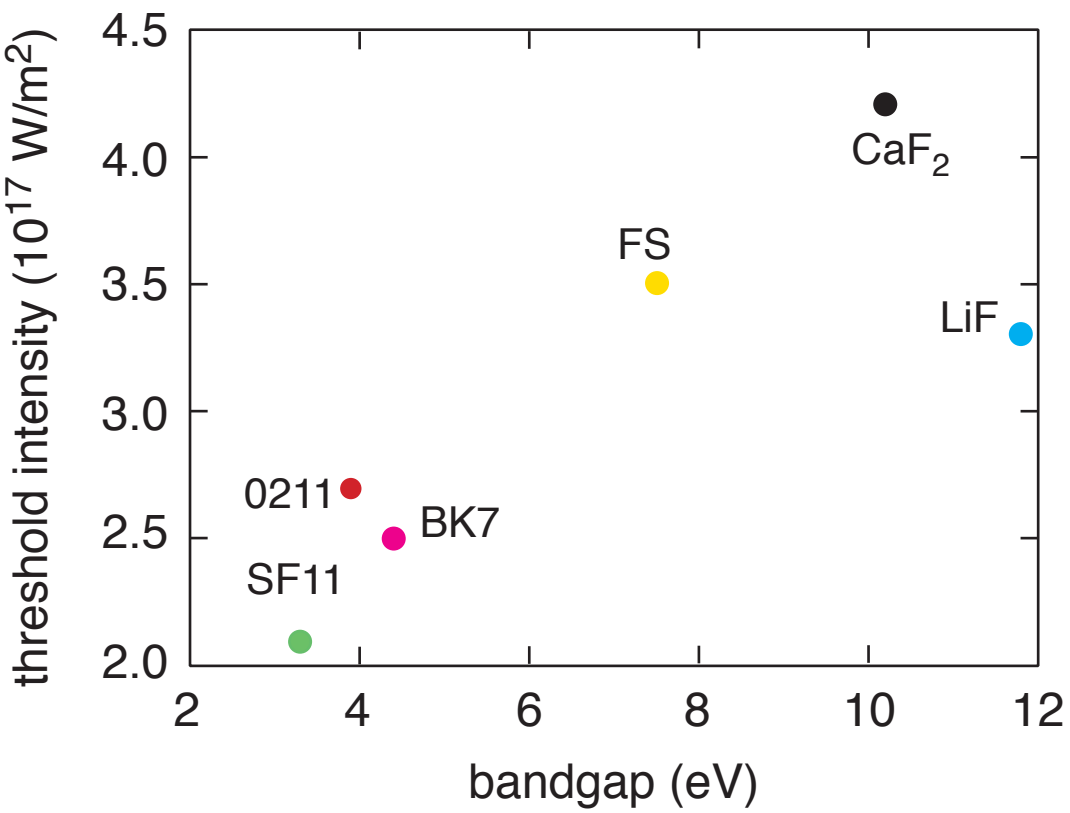
Femtosecond materials interactions

vary material…



Femtosecond materials interactions

…threshold varies with band gap (but not much!)



Femtosecond materials interactions

- nonlinear interaction
- disrupt matter inside bulk
- ablation at very low energy

Outline

- femtosecond materials interactions
- **subcellular surgery**
- nanoneurosurgery

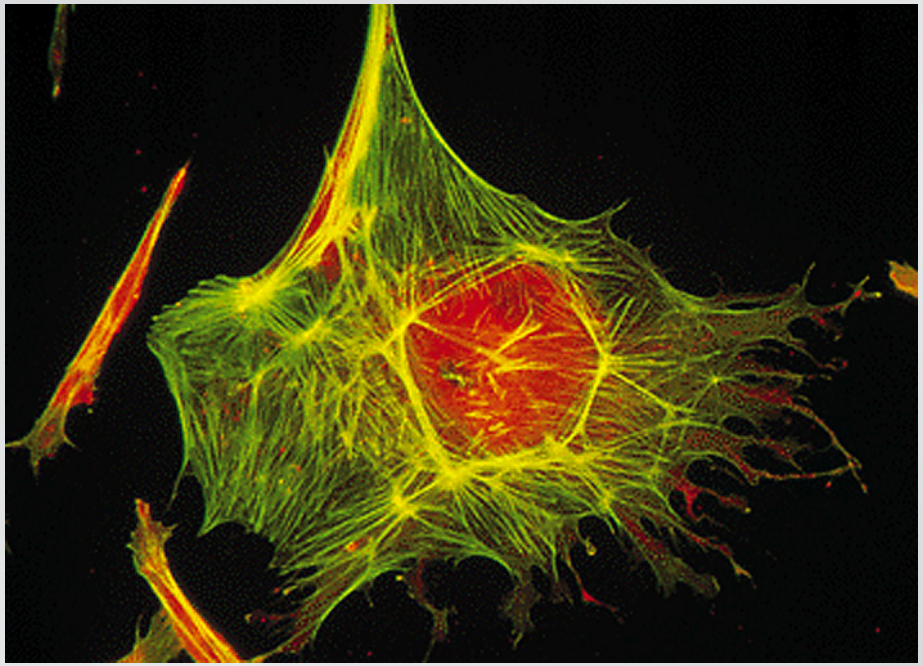
Subcellular surgery

Q: can we ablate material on the subcellular scale?

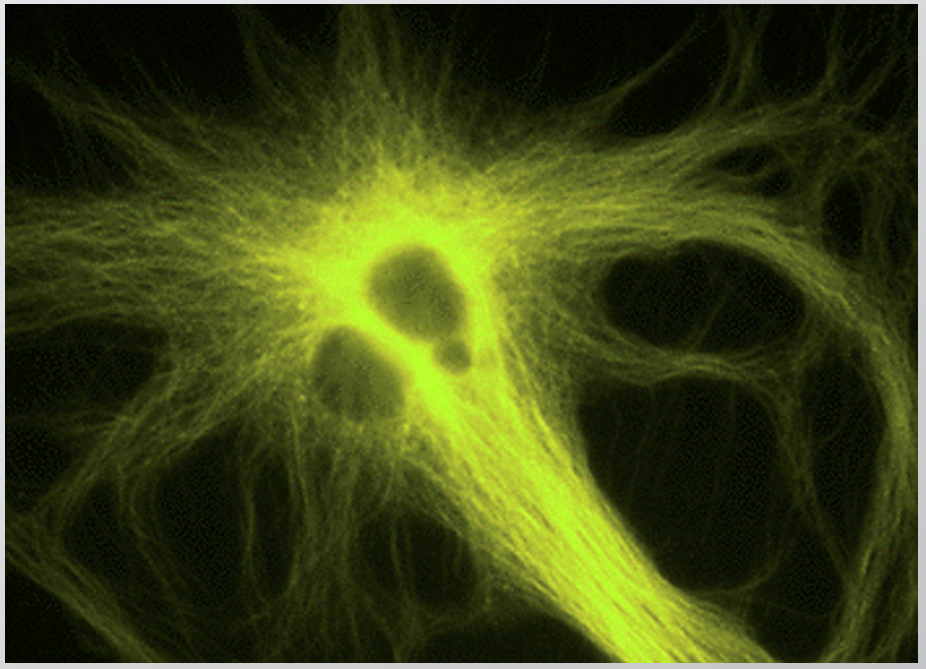
Subcellular surgery

two components

actin fibers



microtubules



Subcellular surgery

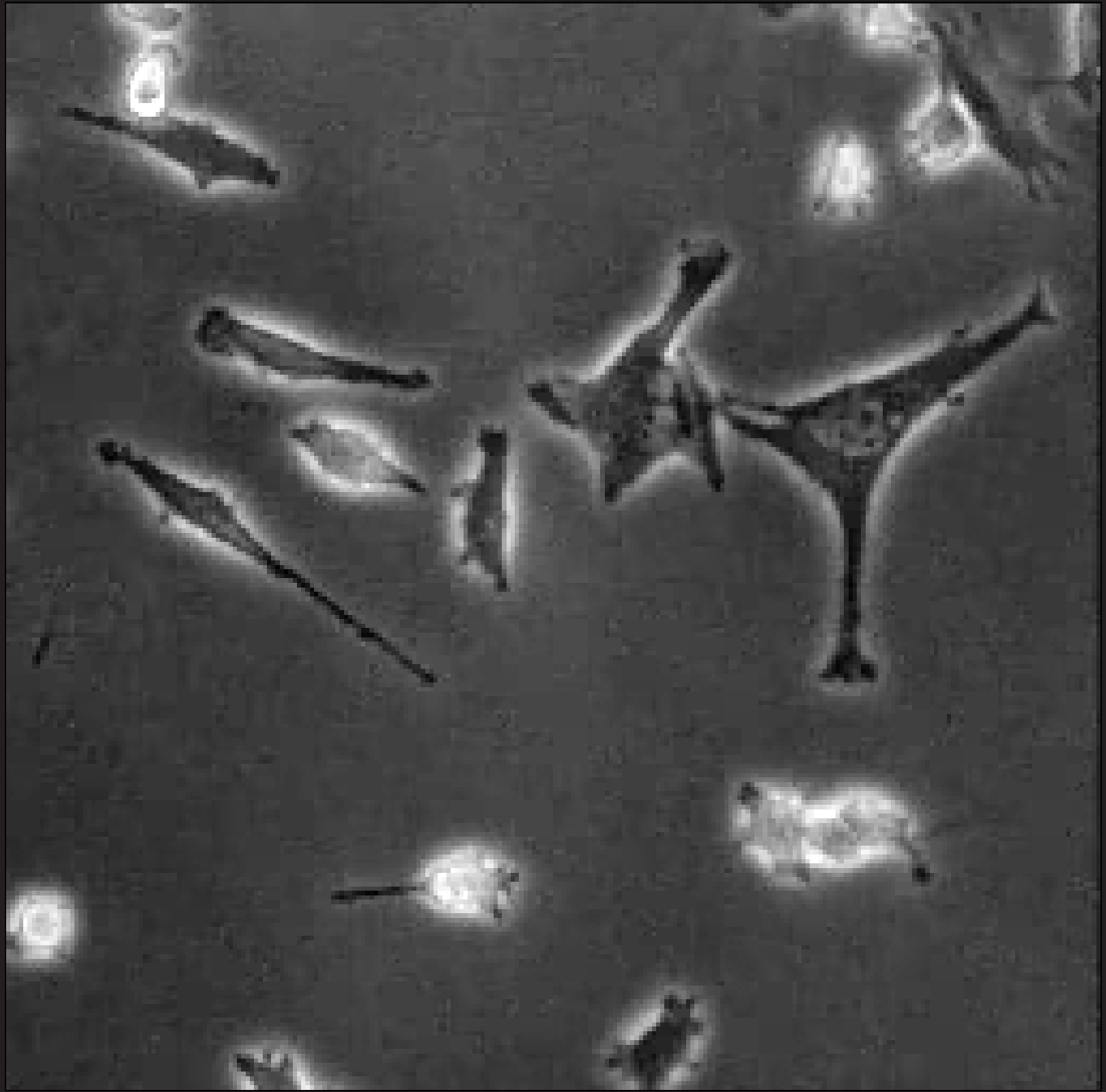
Requirements:

- submicrometer precision (in bulk)
- no damage to neighboring structures
- independent of structure/organelle type

Subcellular surgery

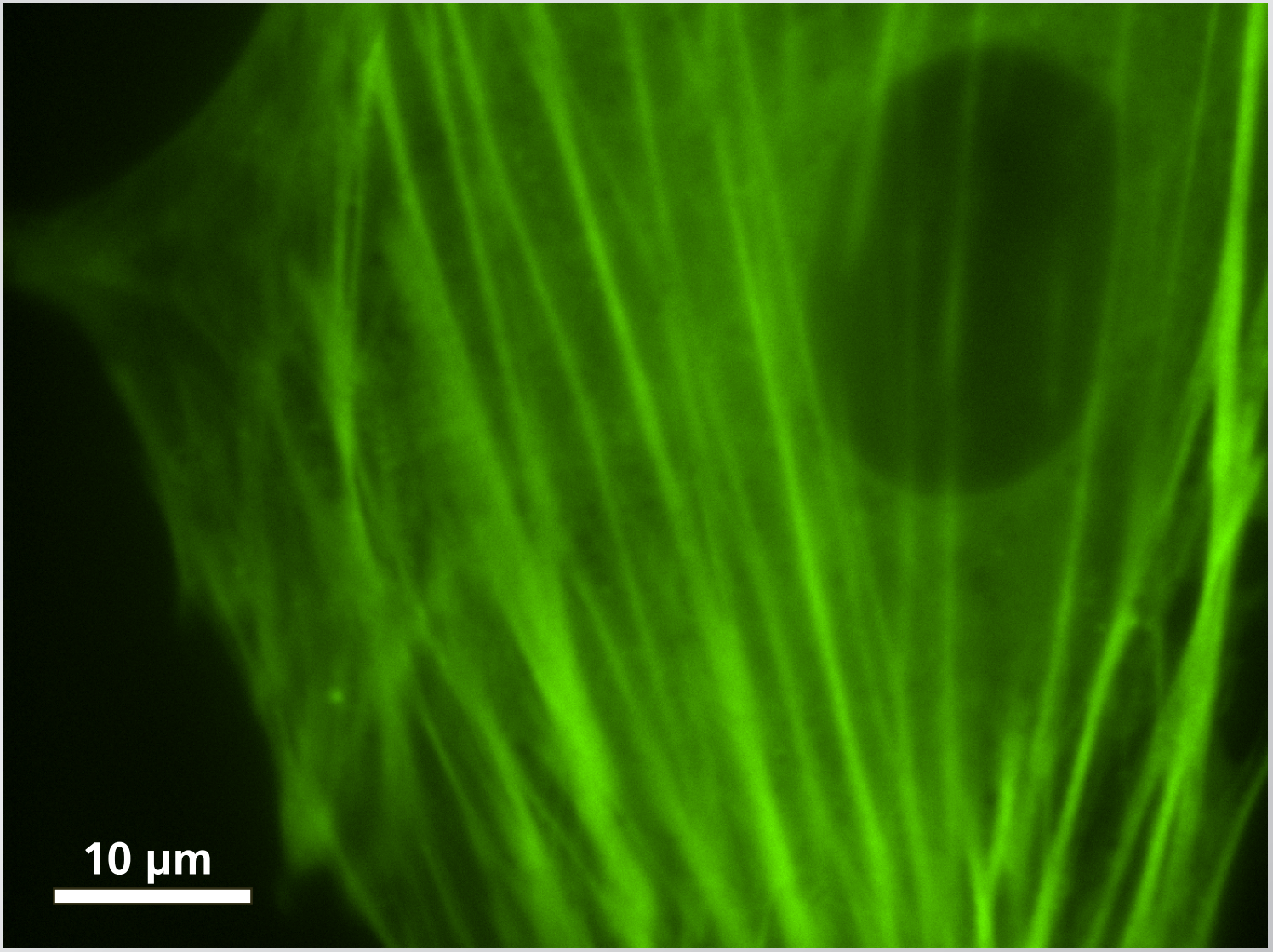
Cytoskeleton

- gives a cell its shape
- provides a scaffold for organelles
- responsible cell motion and attachment
- facilitates intracellular transport and signaling
- required for cell division



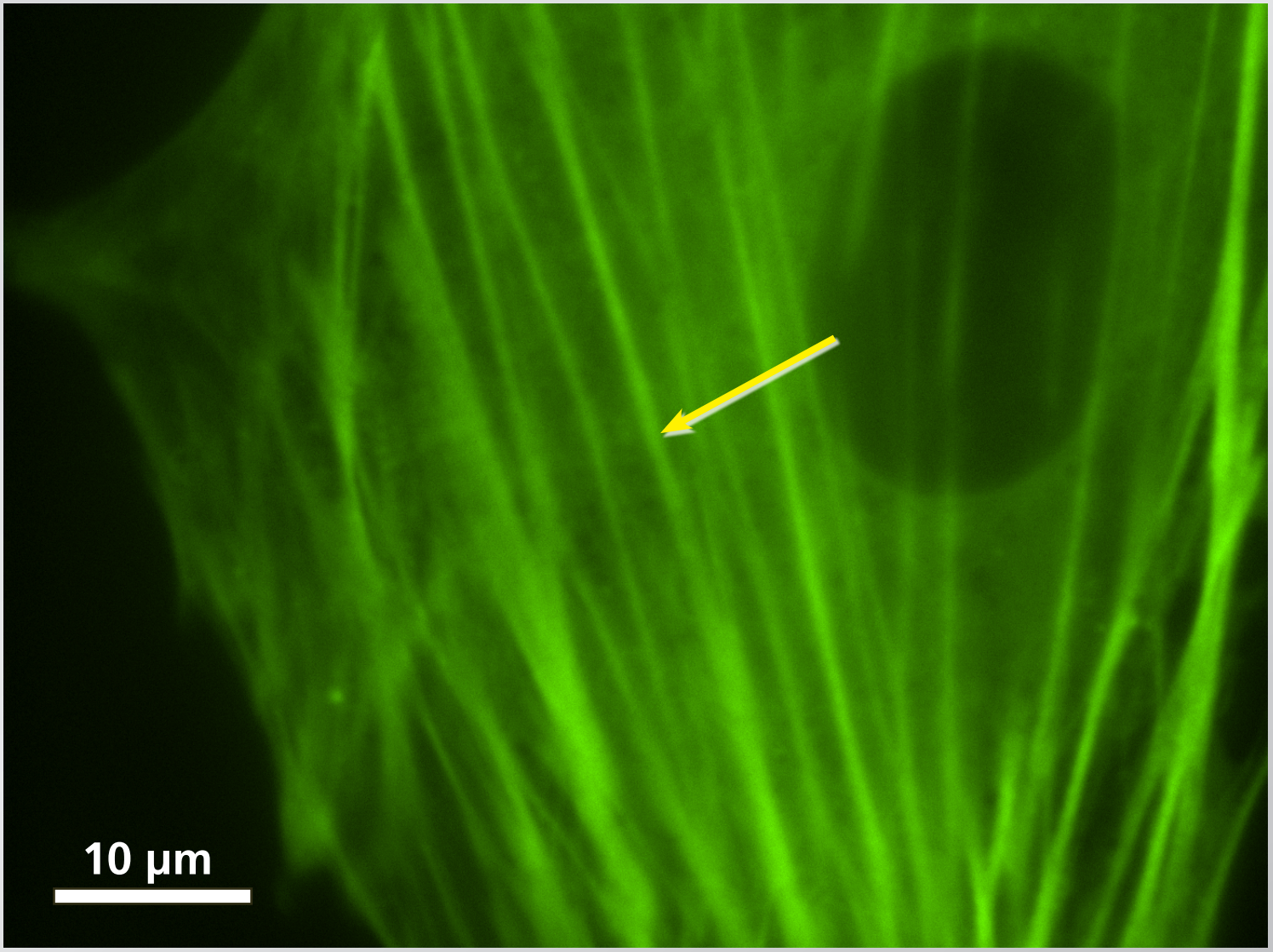
Subcellular surgery

YFP-labeled actin fiber network of a live cell



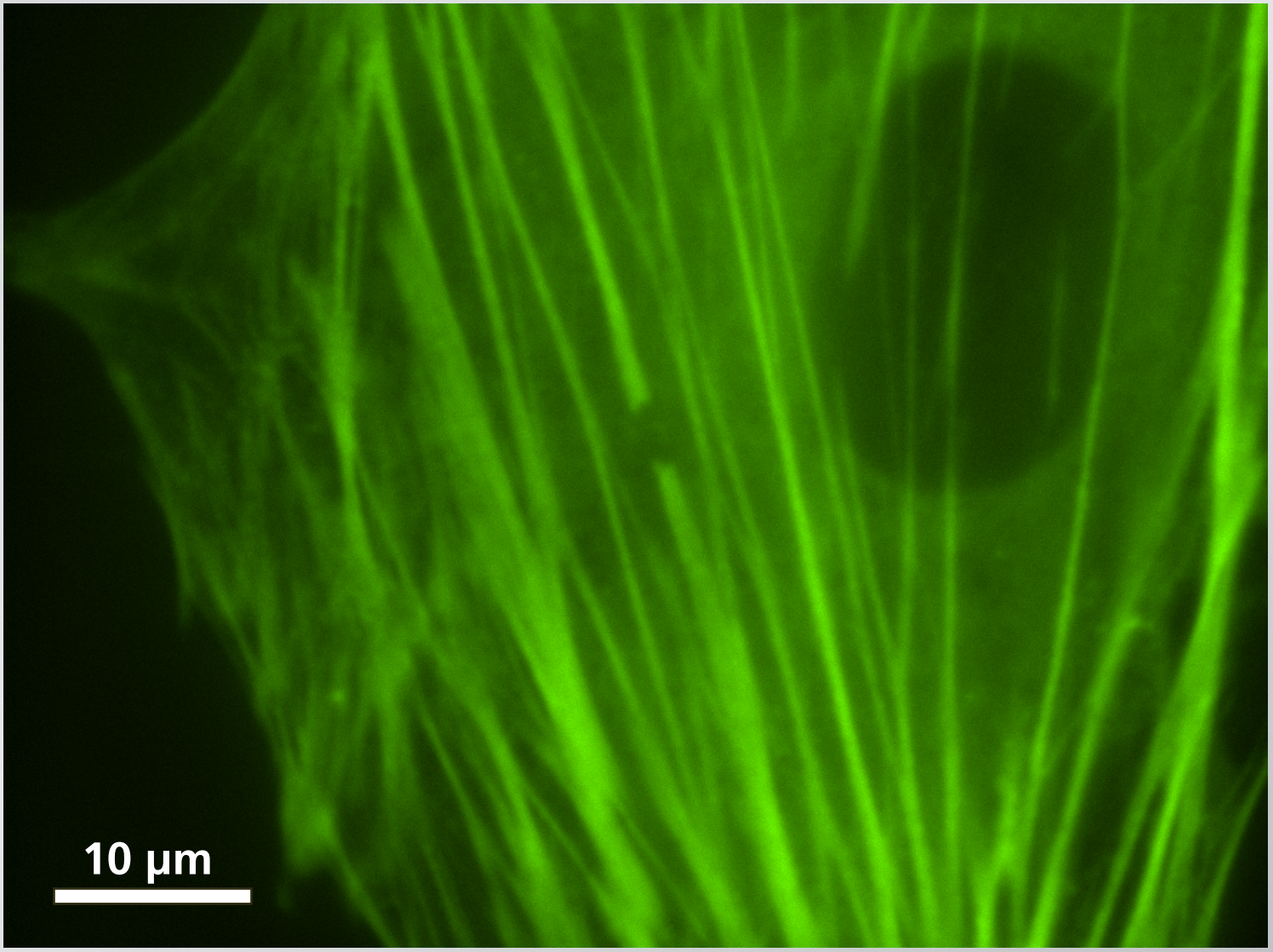
Subcellular surgery

cut a single fiber bundle



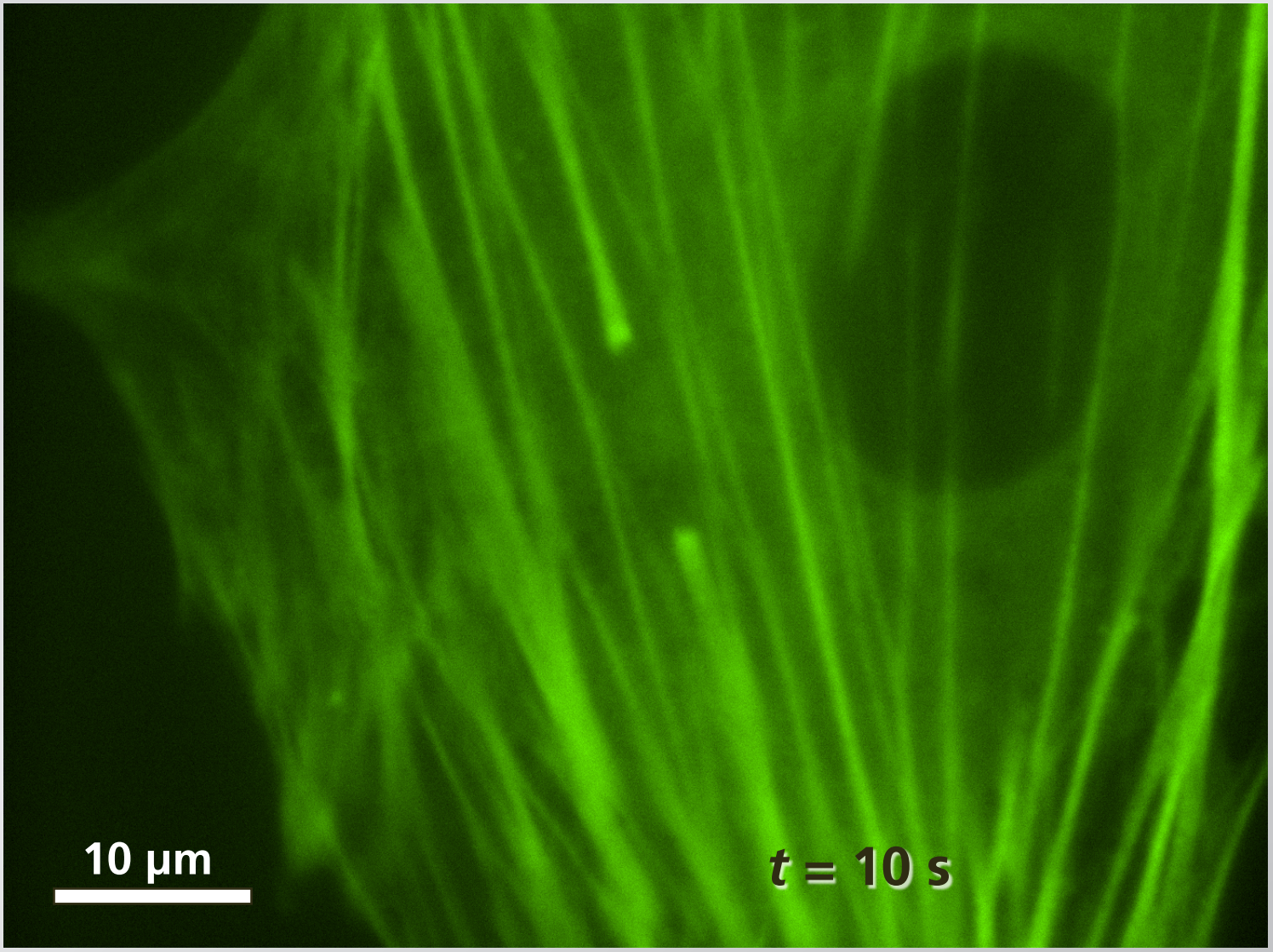
Subcellular surgery

cut a single fiber bundle



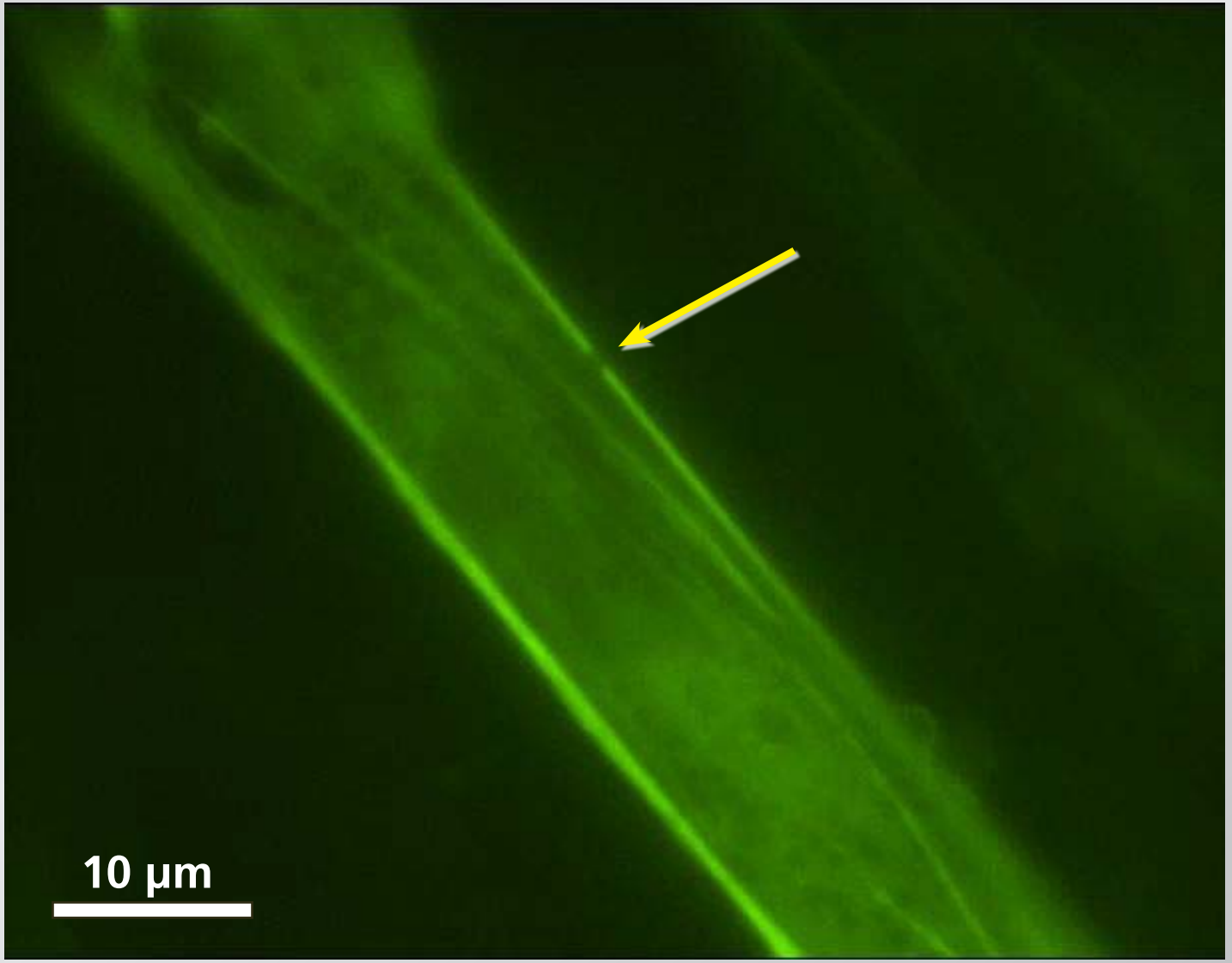
Subcellular surgery

gap widens with time



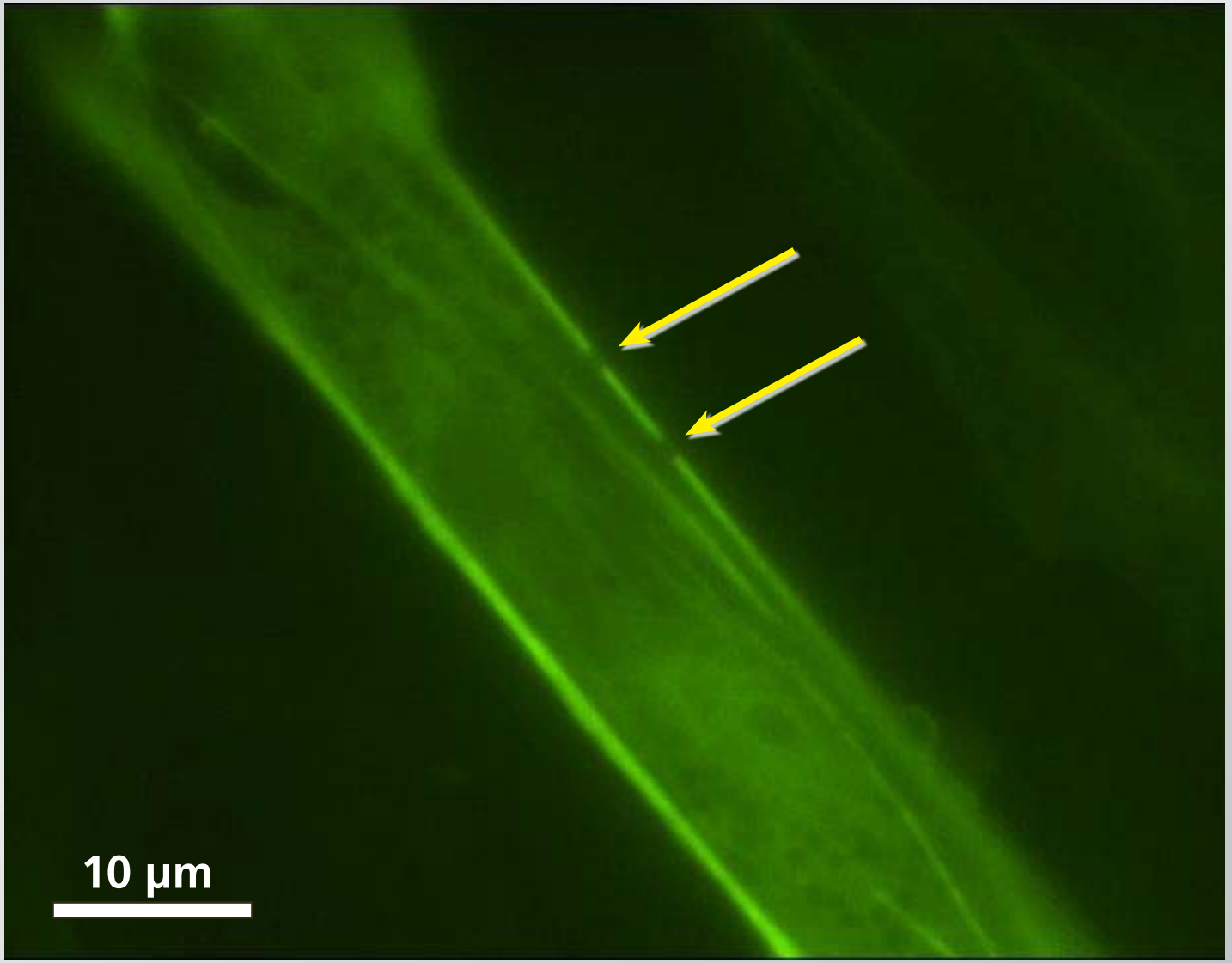
Subcellular surgery

retraction or depolymerization?



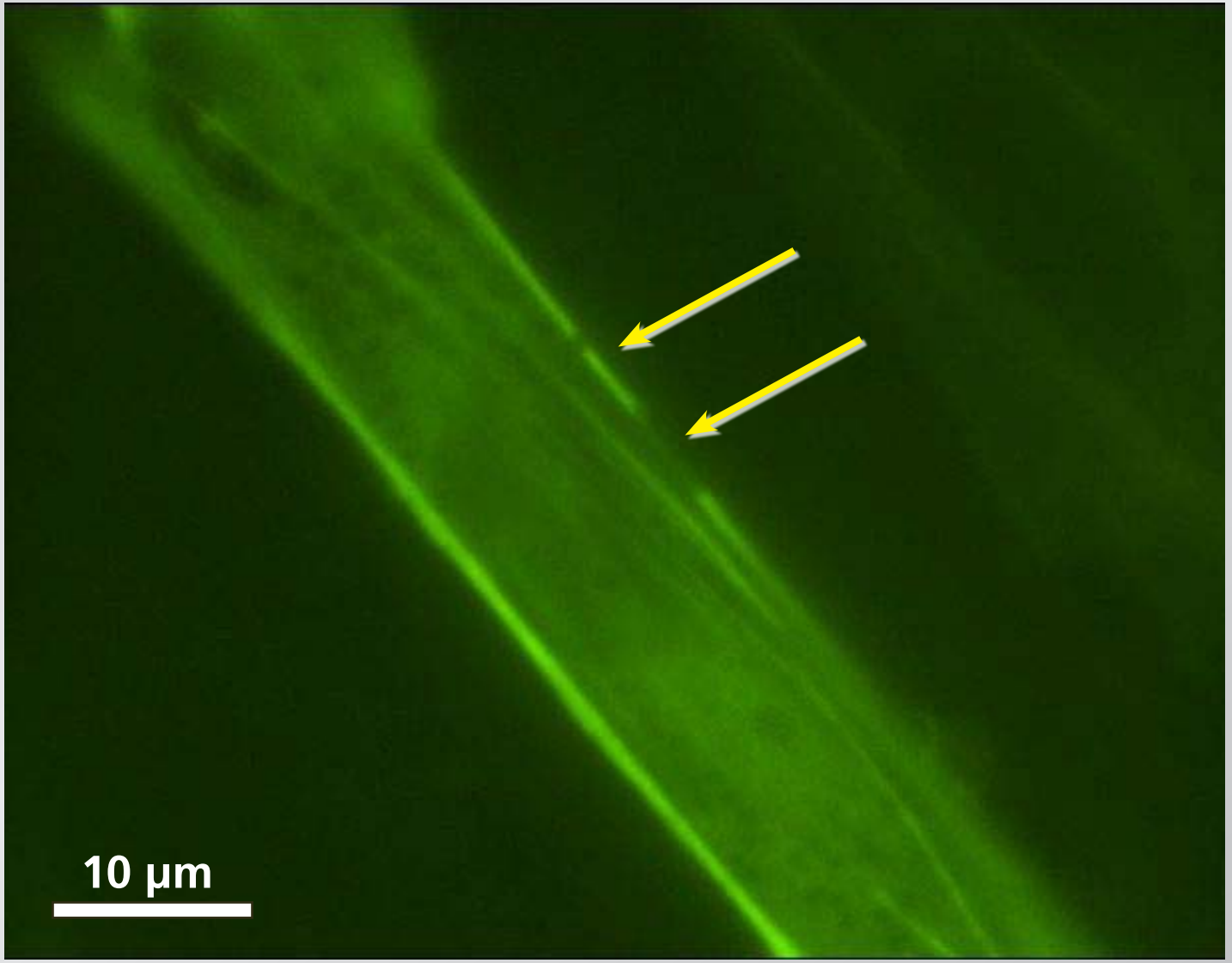
Subcellular surgery

retraction or depolymerization?



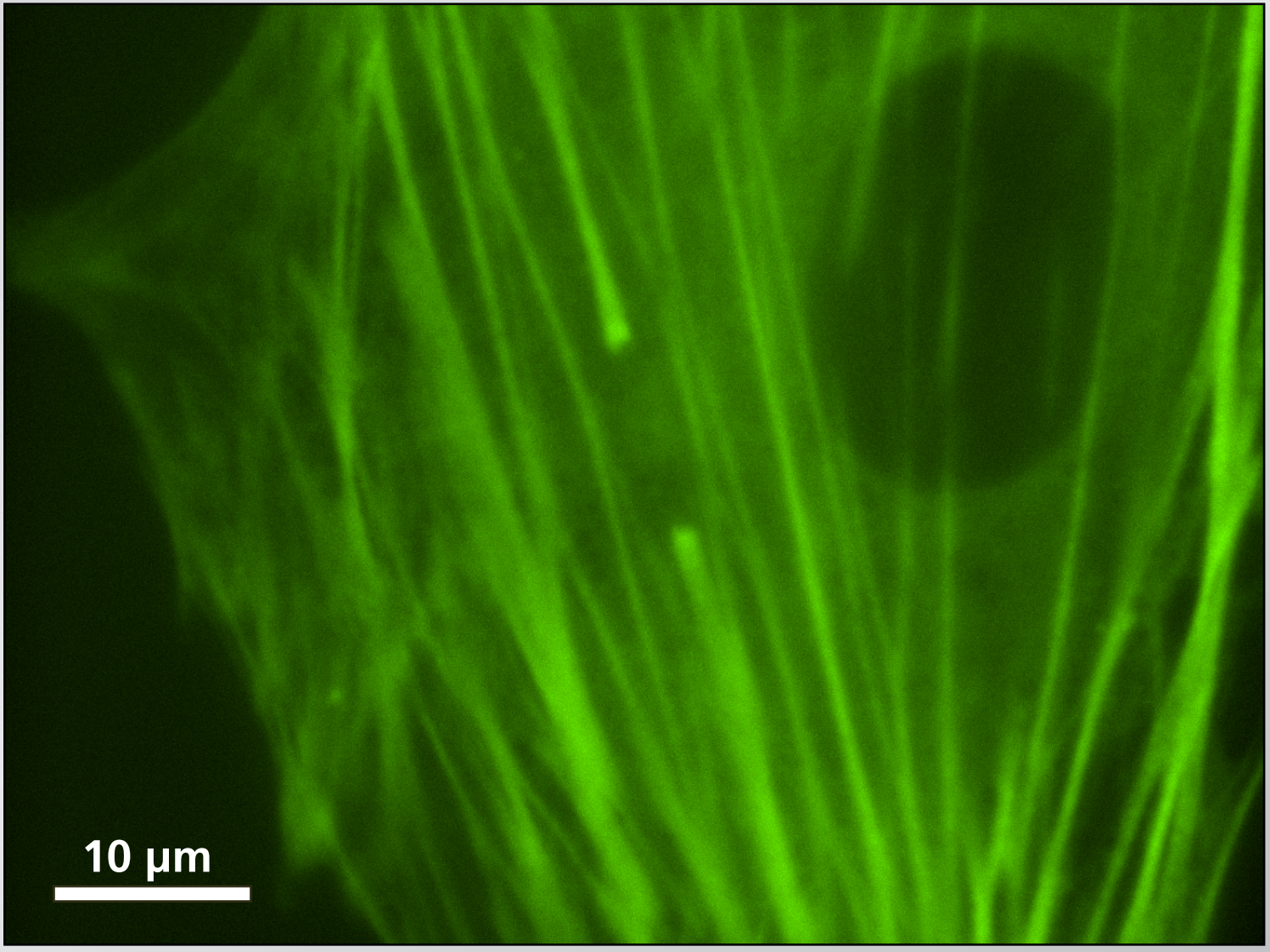
Subcellular surgery

retraction!

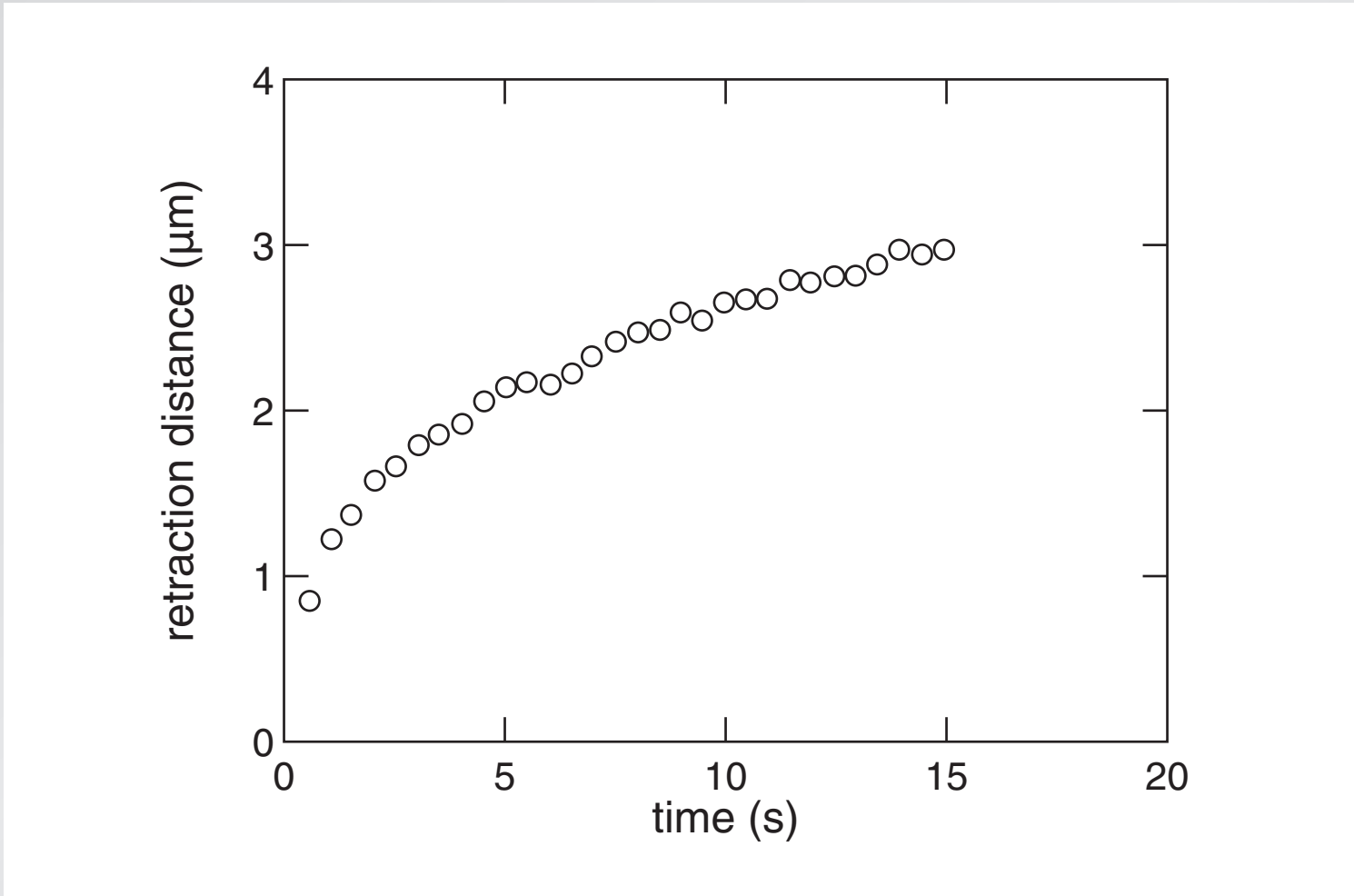


Subcellular surgery

dynamics provides information on *in vivo* mechanics

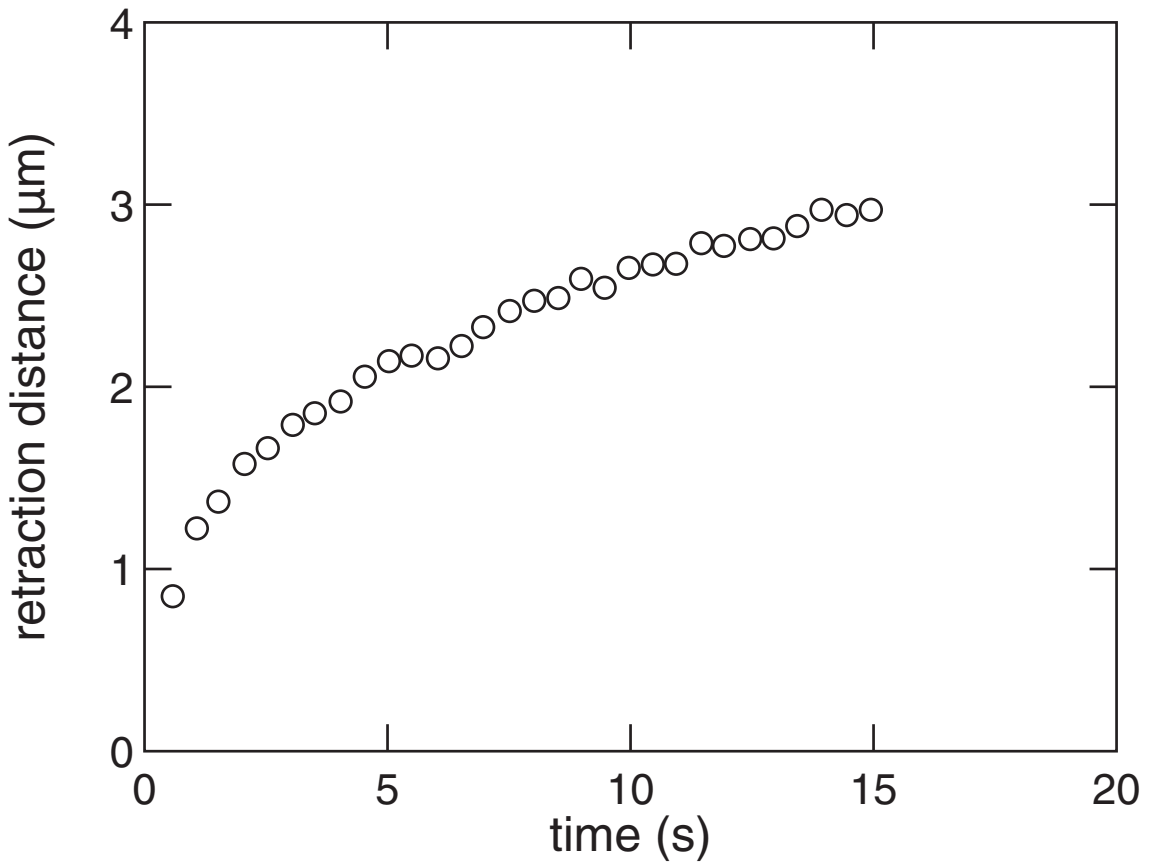


Subcellular surgery



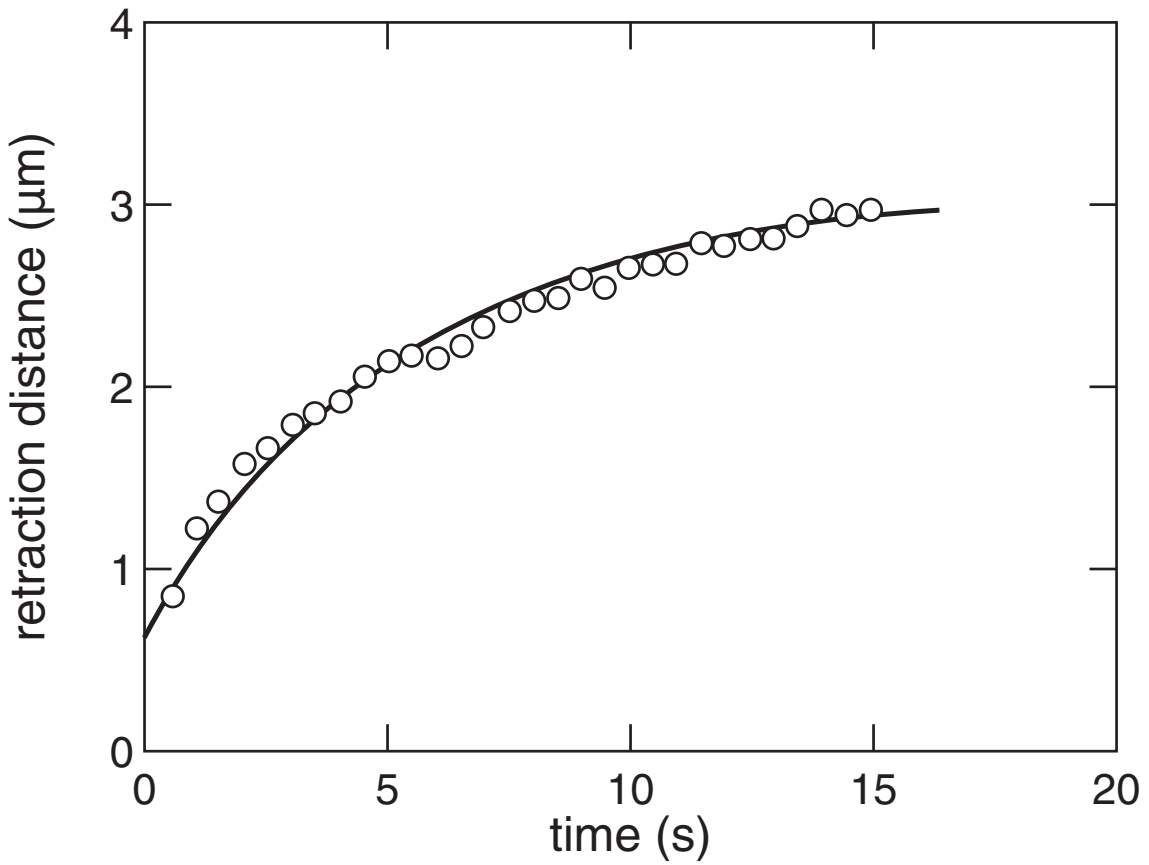
Subcellular surgery

overdamped spring: $\Delta L = L_{\infty}(1 - e^{-t/\tau}) + L_{o}$



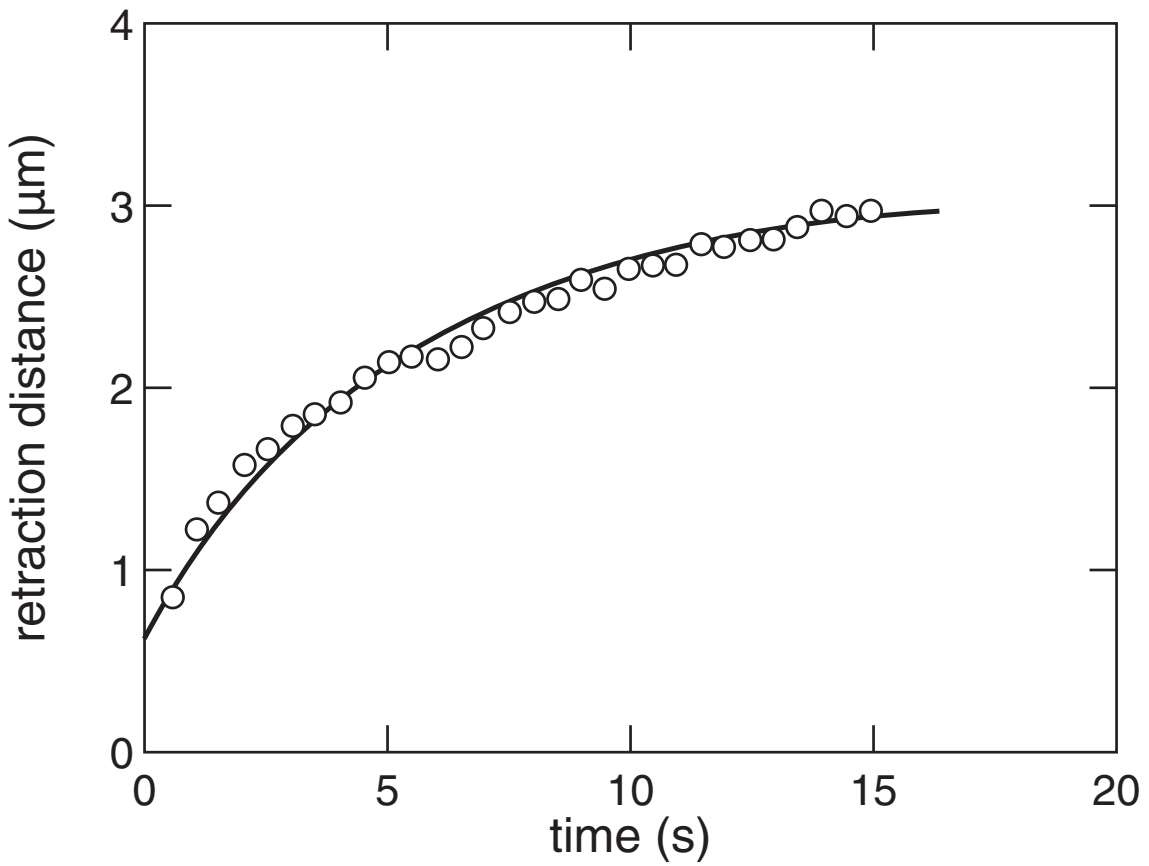
Subcellular surgery

overdamped spring: $\Delta L = L_{\infty}(1 - e^{-t/\tau}) + L_{o}$



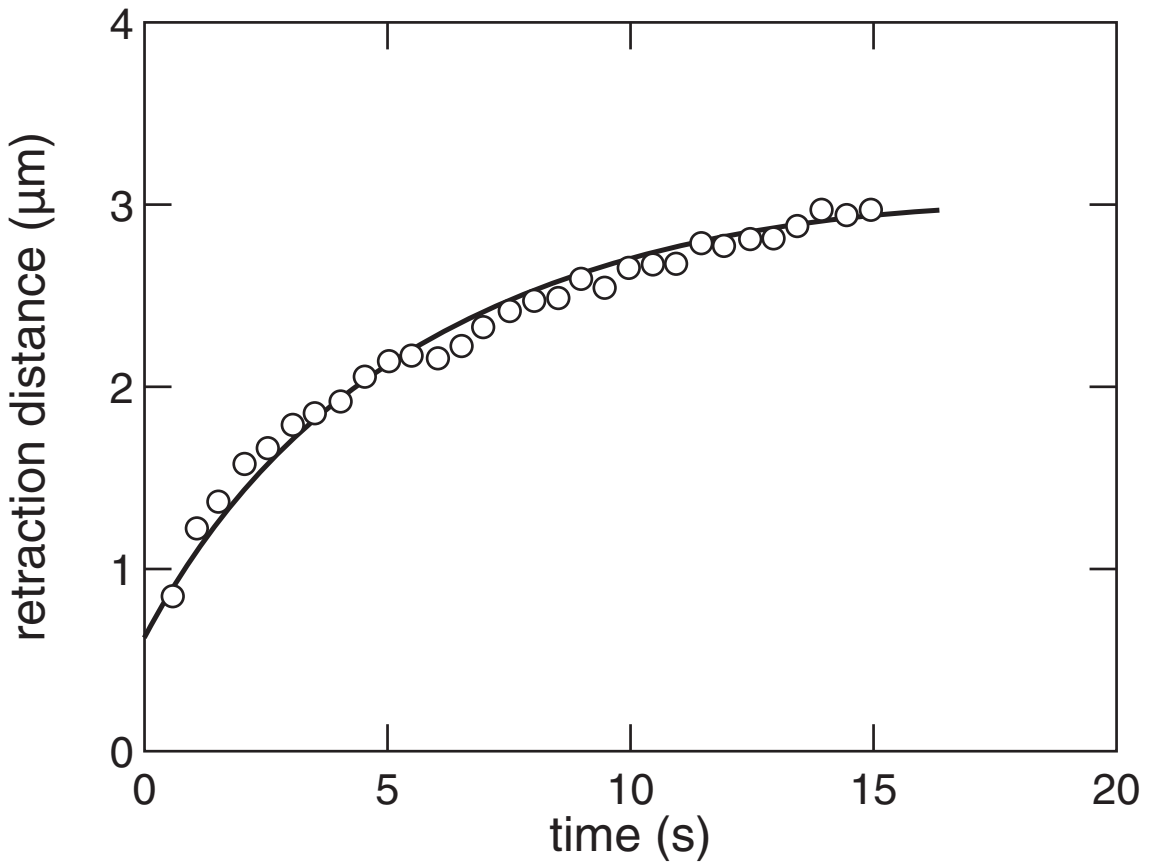
Subcellular surgery

L_o and τ independent of fiber width!



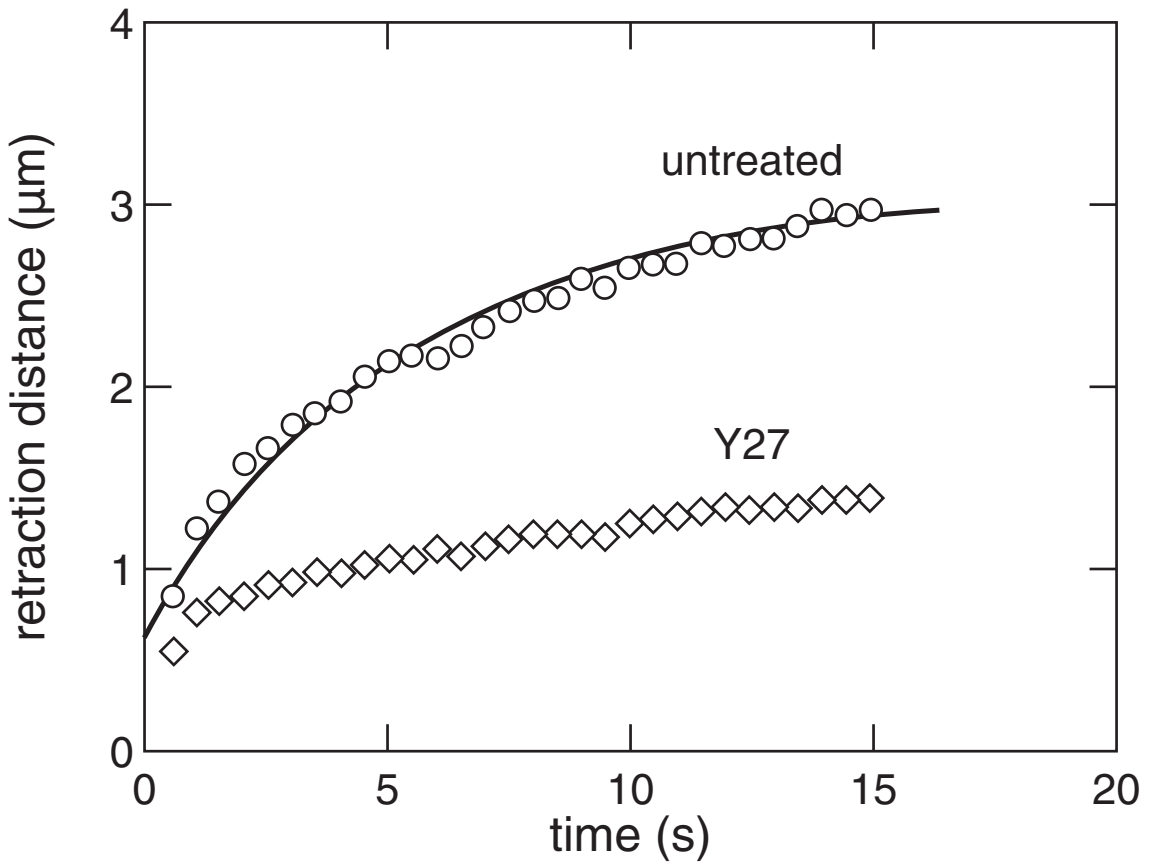
Subcellular surgery

tension in actin filaments is generated by myosin motors



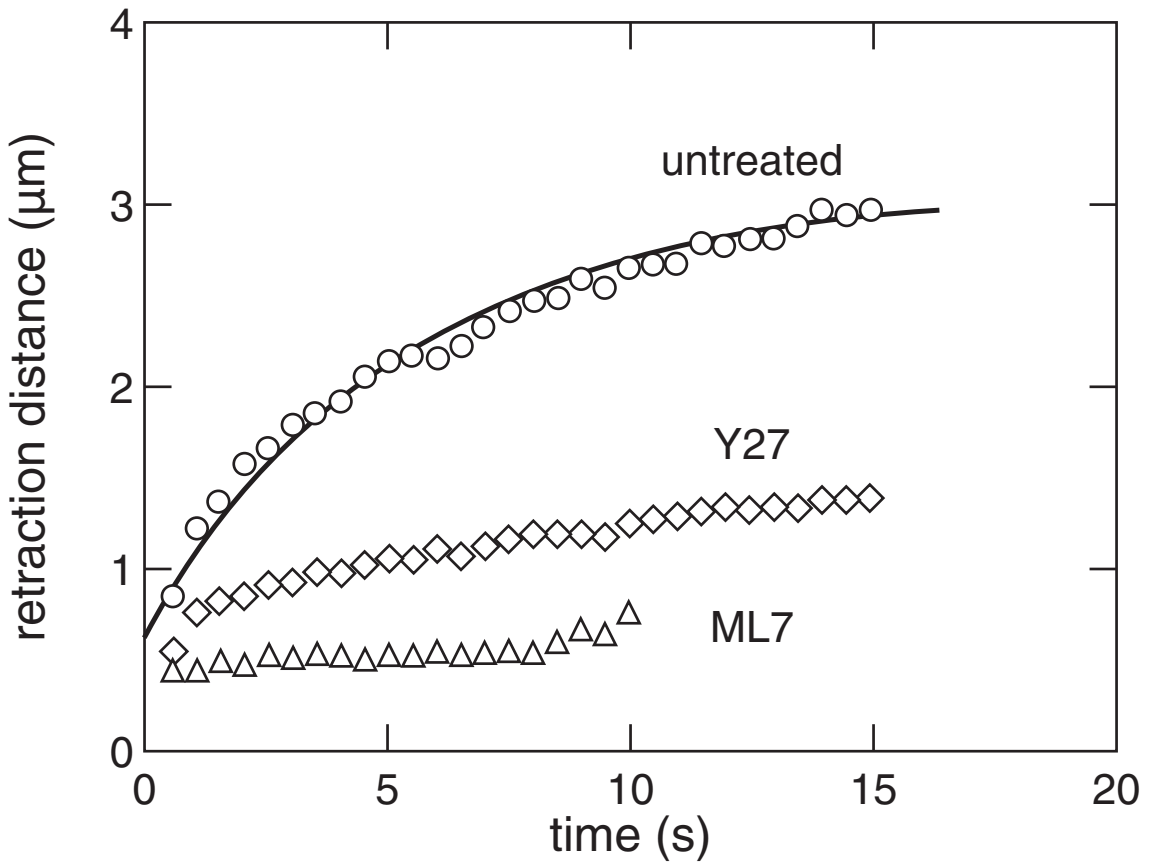
Subcellular surgery

Y27: inhibits some myosin activity



Subcellular surgery

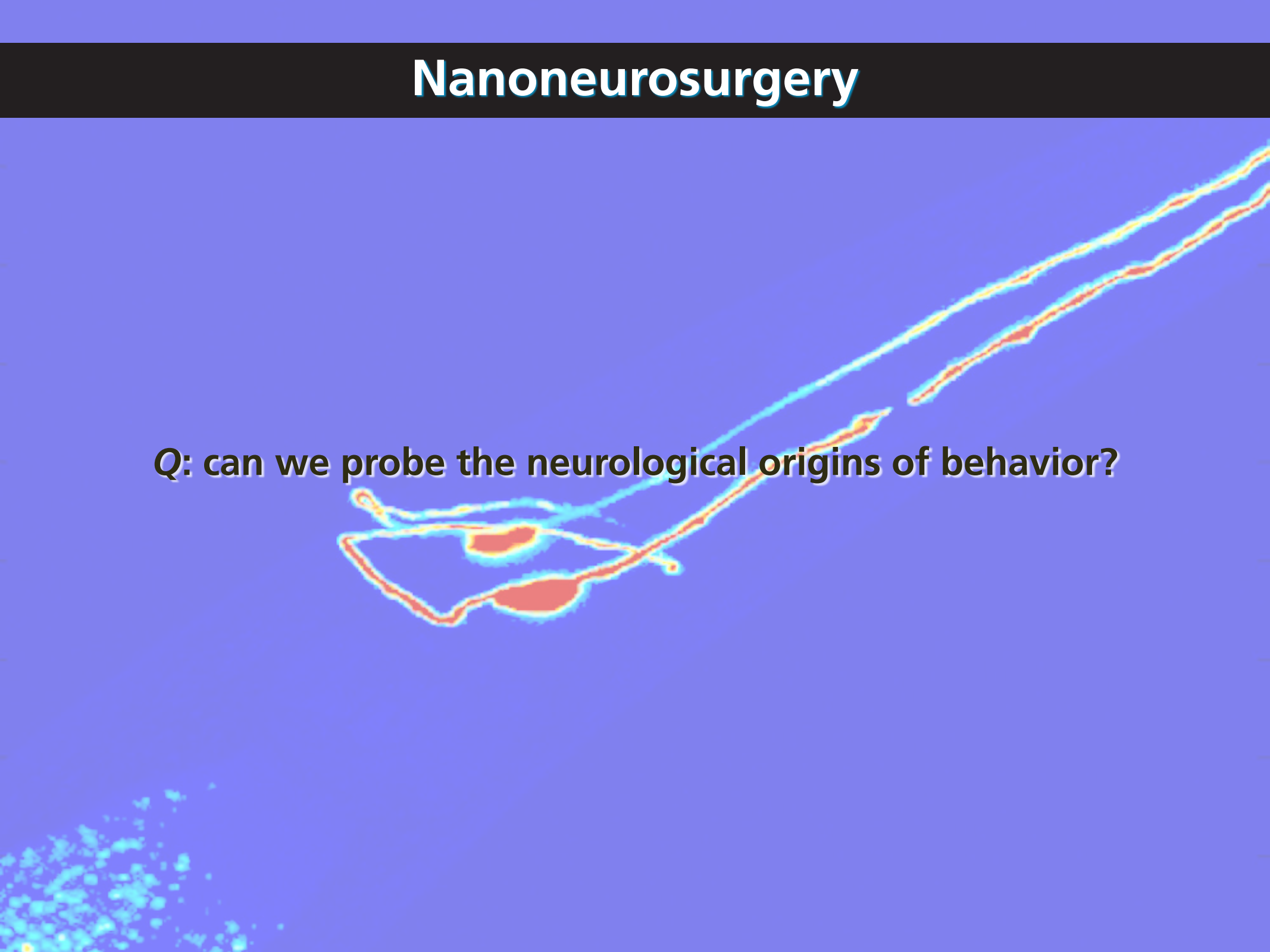
ML7: direct inhibitor of myosin activity



Outline

- femtosecond materials interactions
- subcellular surgery
- **nanoneurosurgery**

Nanoneurosurgery



Q: can we probe the neurological origins of behavior?

Nanoneurosurgery

Caenorhabditis elegans

Juergen Berger & Ralph Sommer
Max-Planck Institute for Developmental Biology

Nanoneurosurgery

Caenorhabditis elegans

- simple model organism
- similarities to higher organisms
- genome fully sequenced
- easy to handle

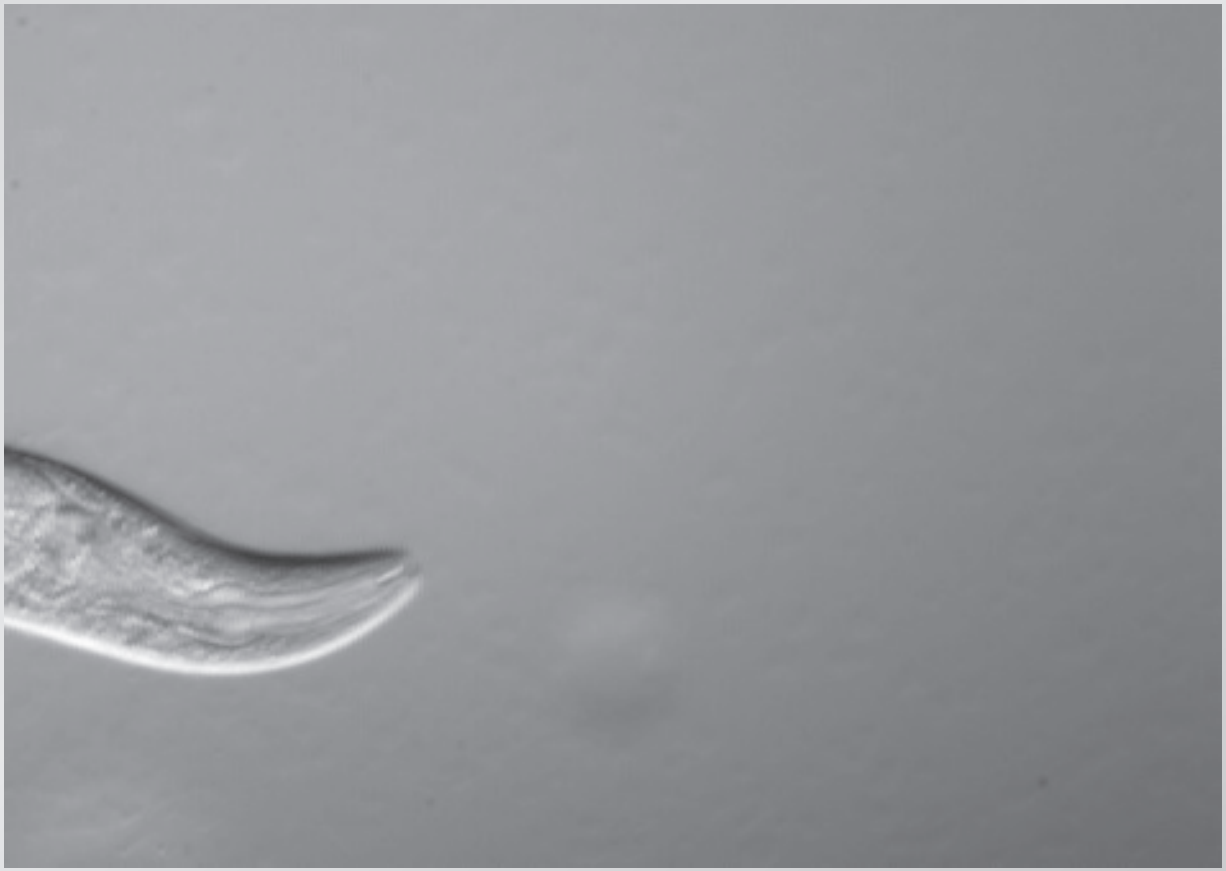
Nanoneurosurgery

Caenorhabditis elegans

- 80 µm x 1 mm
- about 1000 cells
- 302 neurons
- invariant wiring diagram
- neuronal system completely encodes behavior

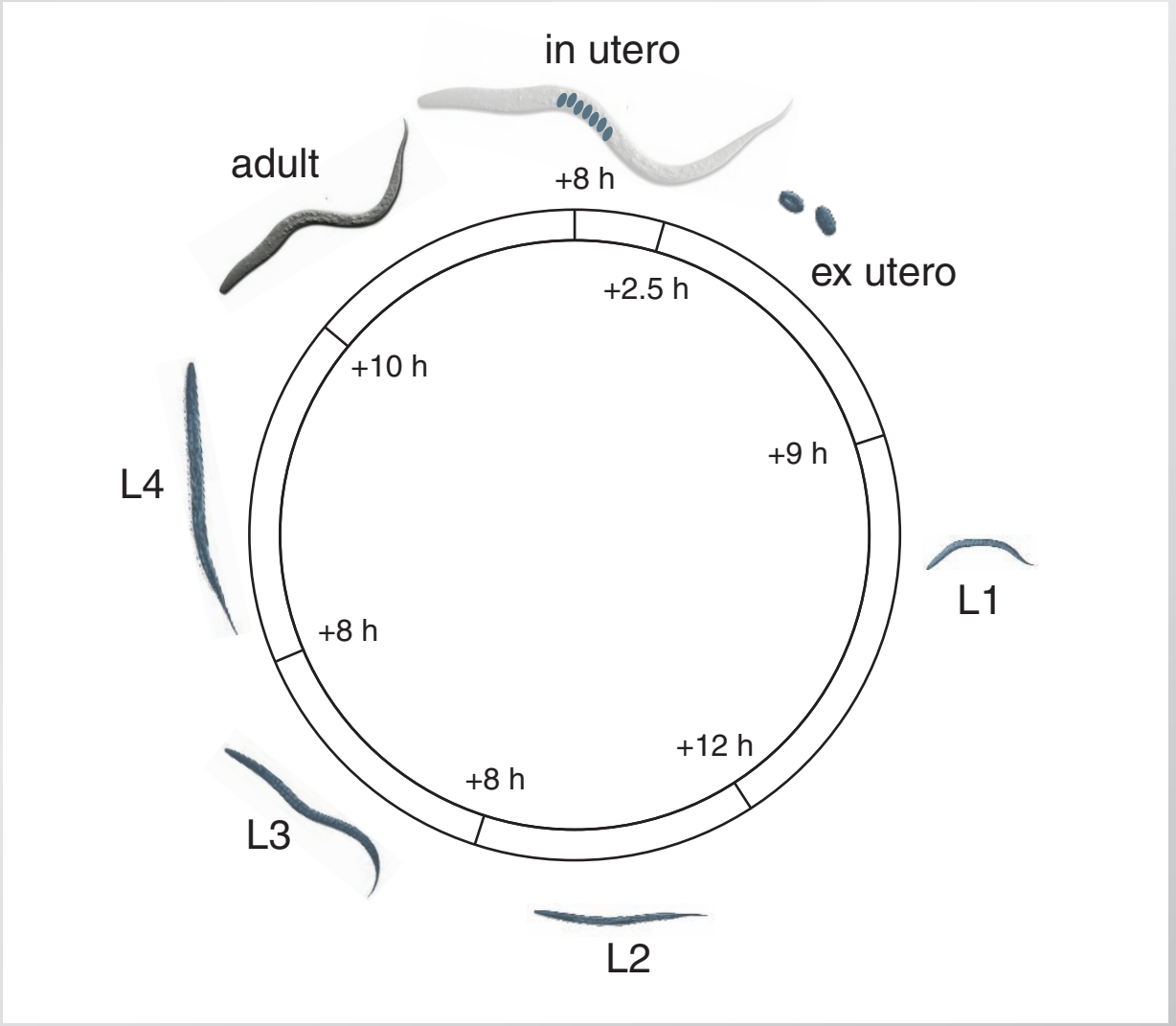
Nanoneurosurgery

Caenorhabditis elegans



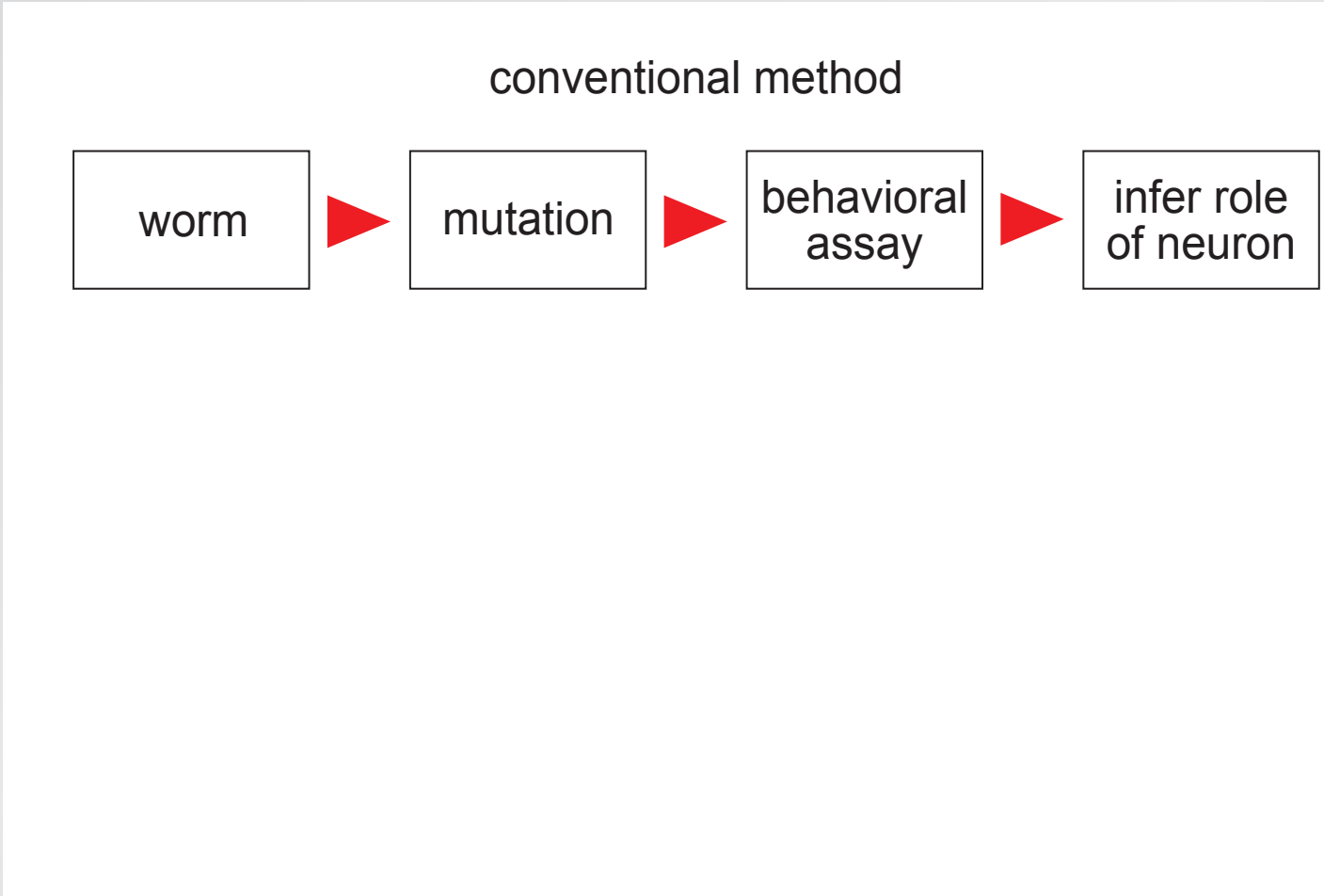
Nanoneurosurgery

C. elegans life cycle



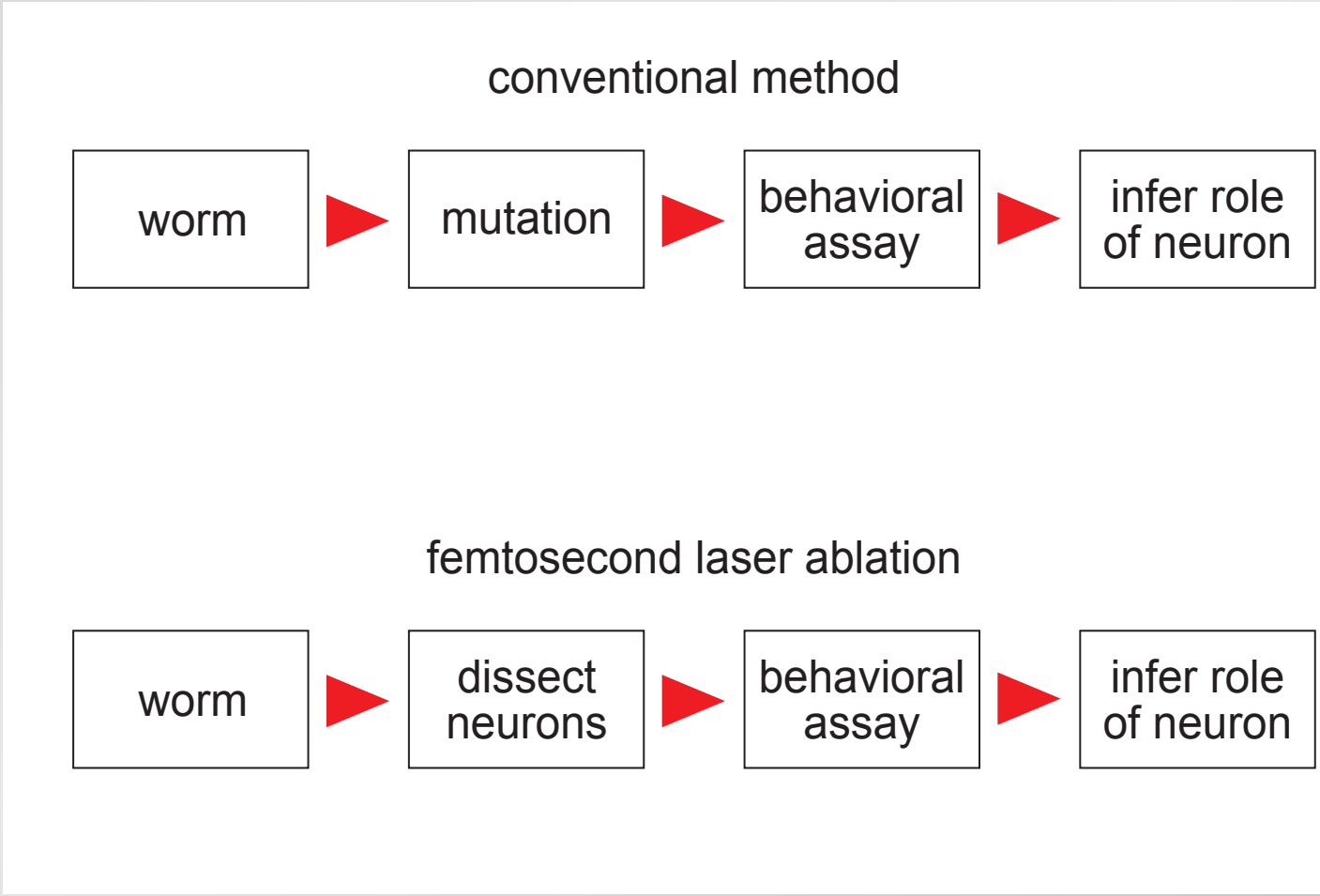
Nanoneurosurgery

Mapping behavior to neurons



Nanoneurosurgery

Mapping behavior to neurons



Nanoneurosurgery

ASH neurons

- responsible for chemical sensing
- ciliary projections extend through skin
- one on each side

Nanoneurosurgery

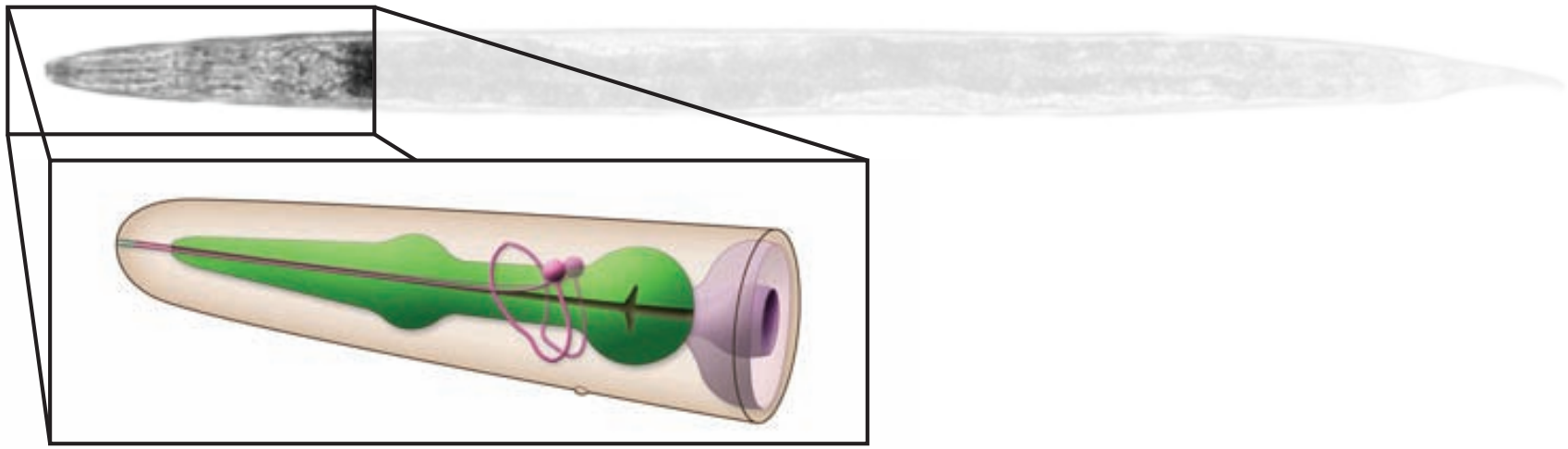
ASH neurons

Nanoneurosurgery

ASH neurons

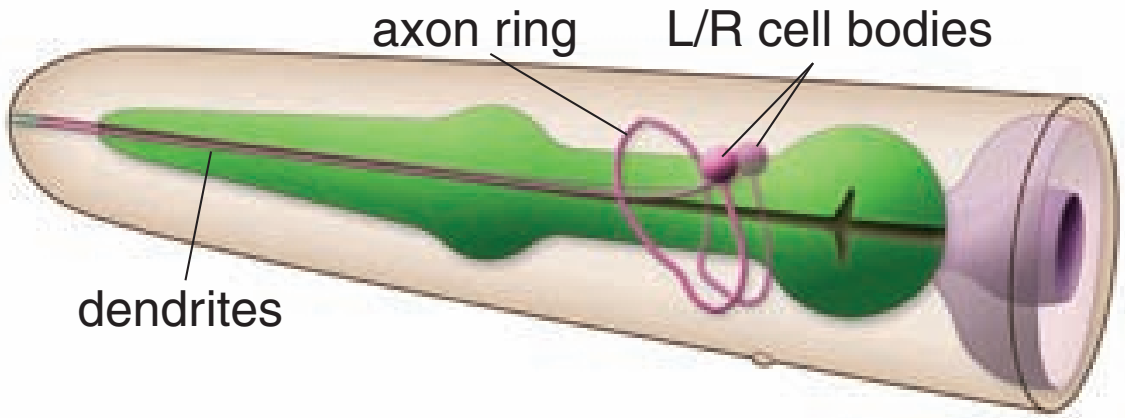
Nanoneurosurgery

ASH neurons



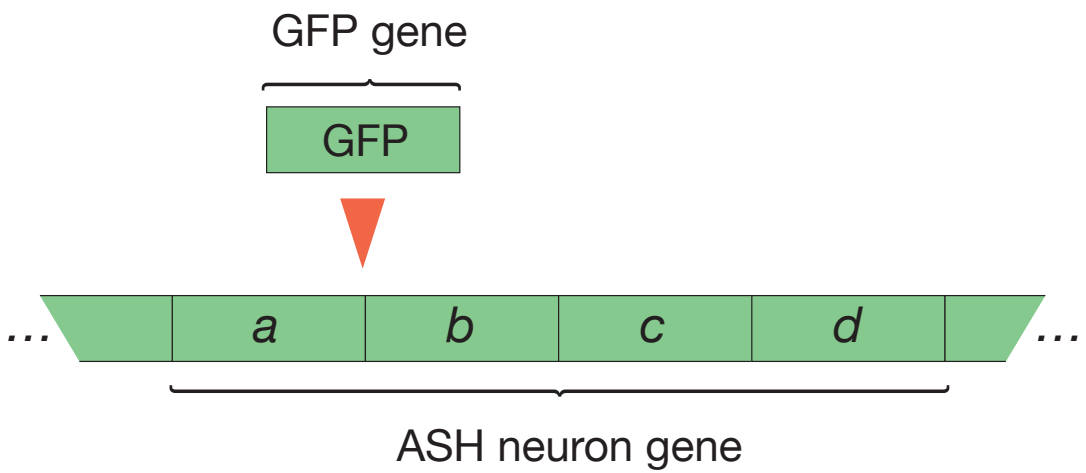
Nanoneurosurgery

ASH neurons



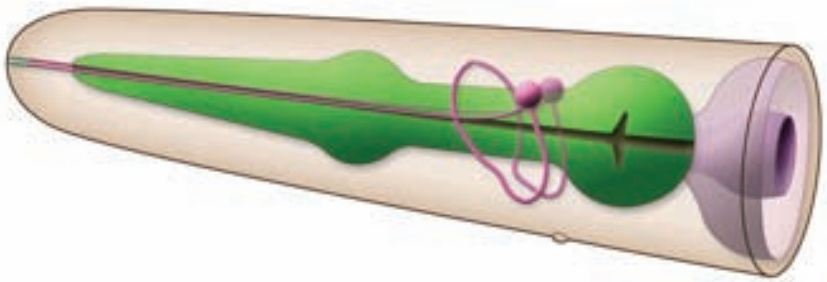
Nanoneurosurgery

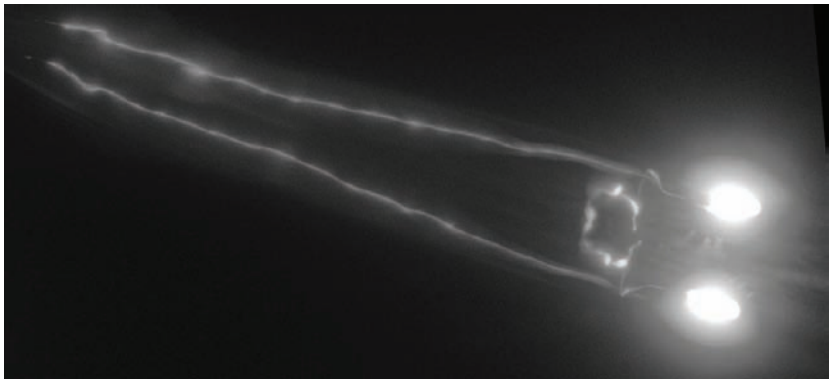
make ASH neurons express GFP



Nanoneurosurgery

make ASH neurons express GFP





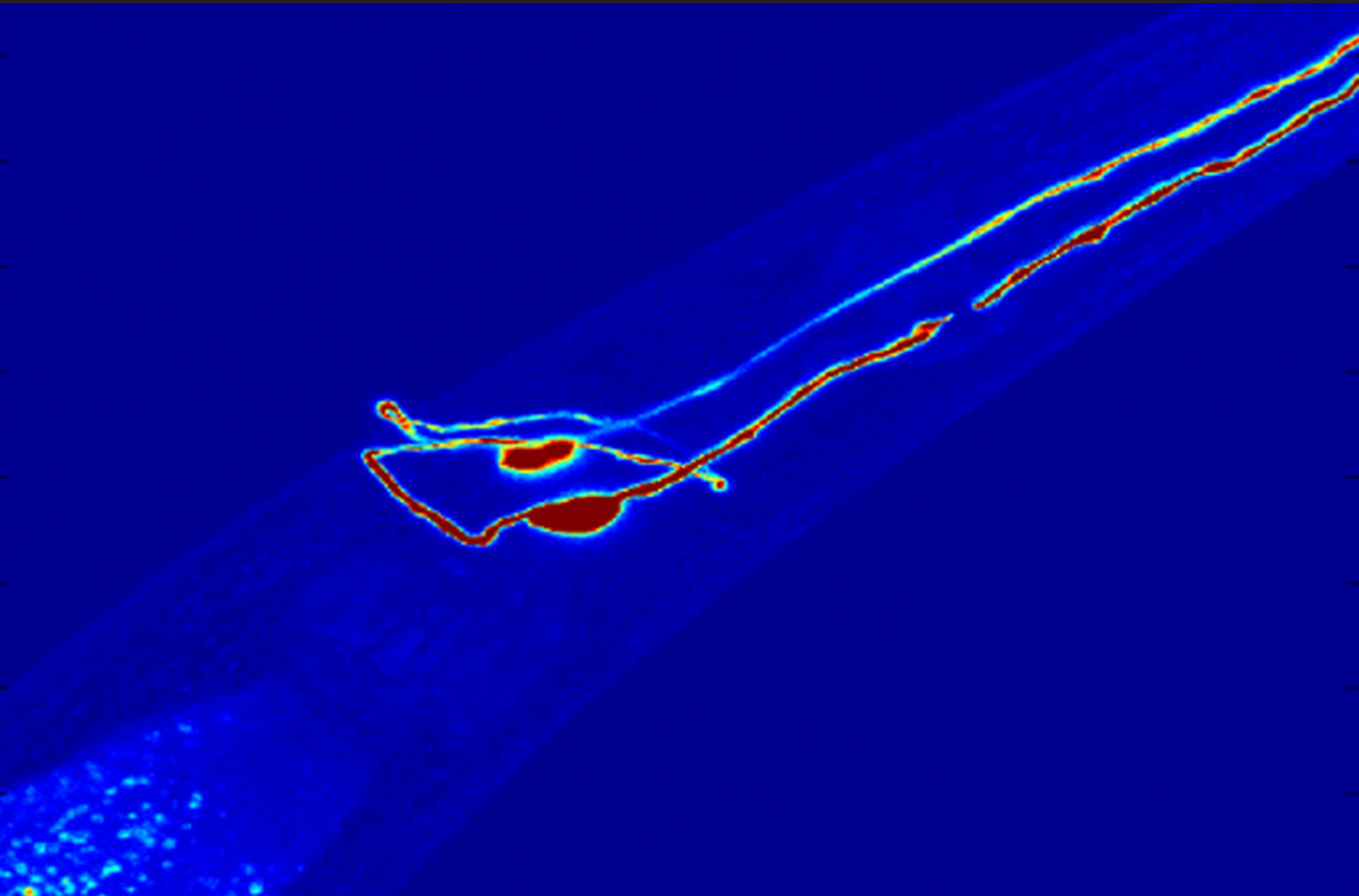
Nanoneurosurgery

GFP: absorbs UV, emits green

Nanoneurosurgery

revive worm, reimage 1 day later

Nanoneurosurgery

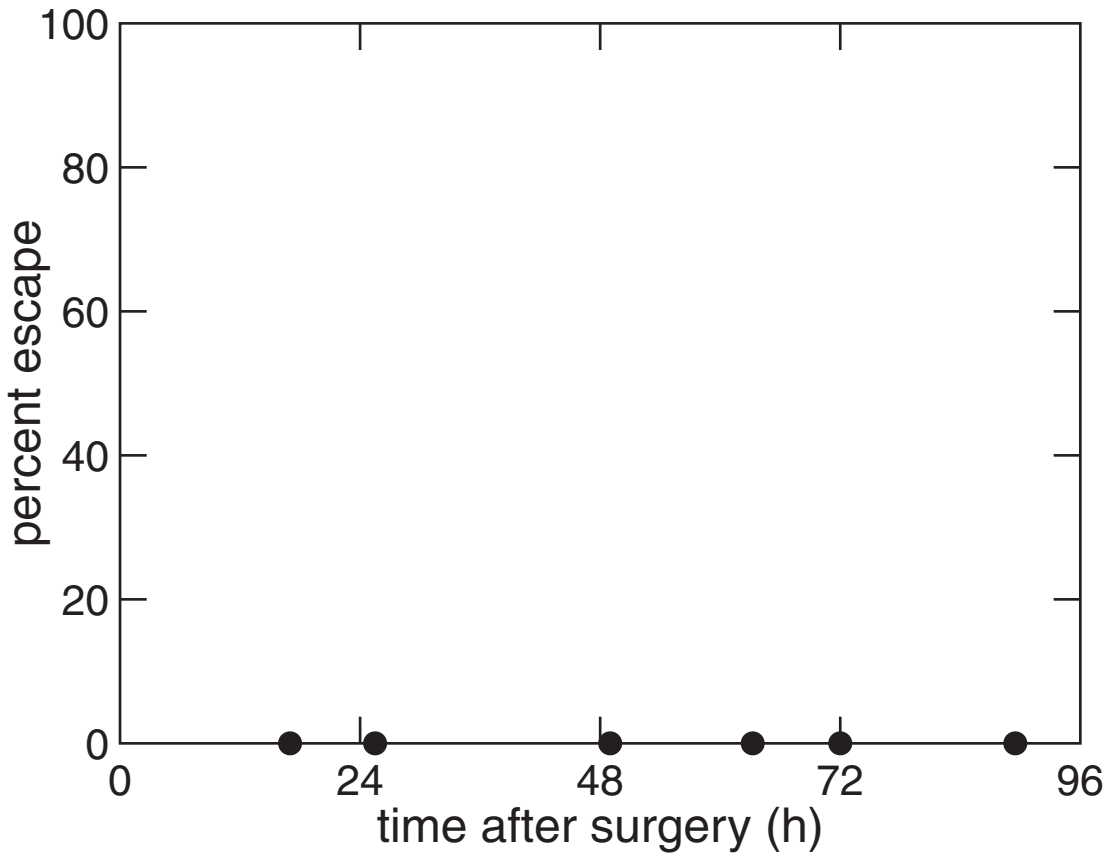


Nanoneurosurgery

osmolarity assay

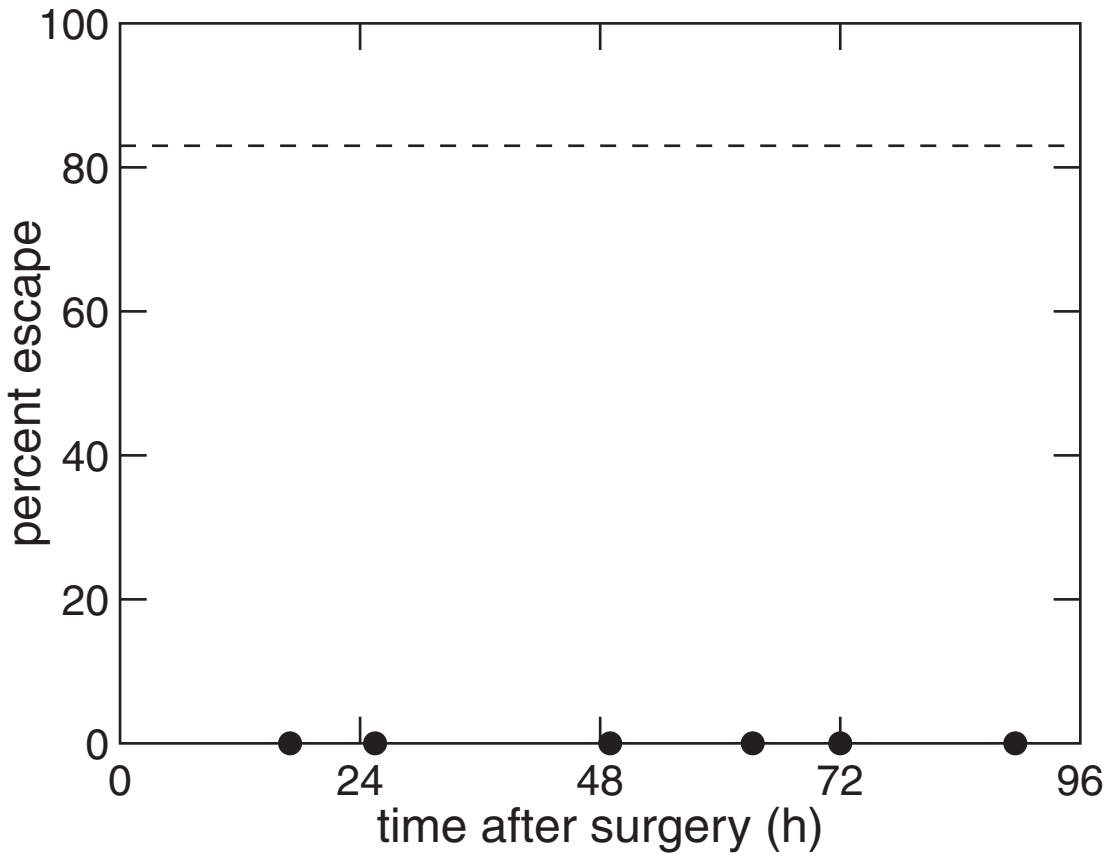
Nanoneurosurgery

escape rate after ‘mock’ surgery



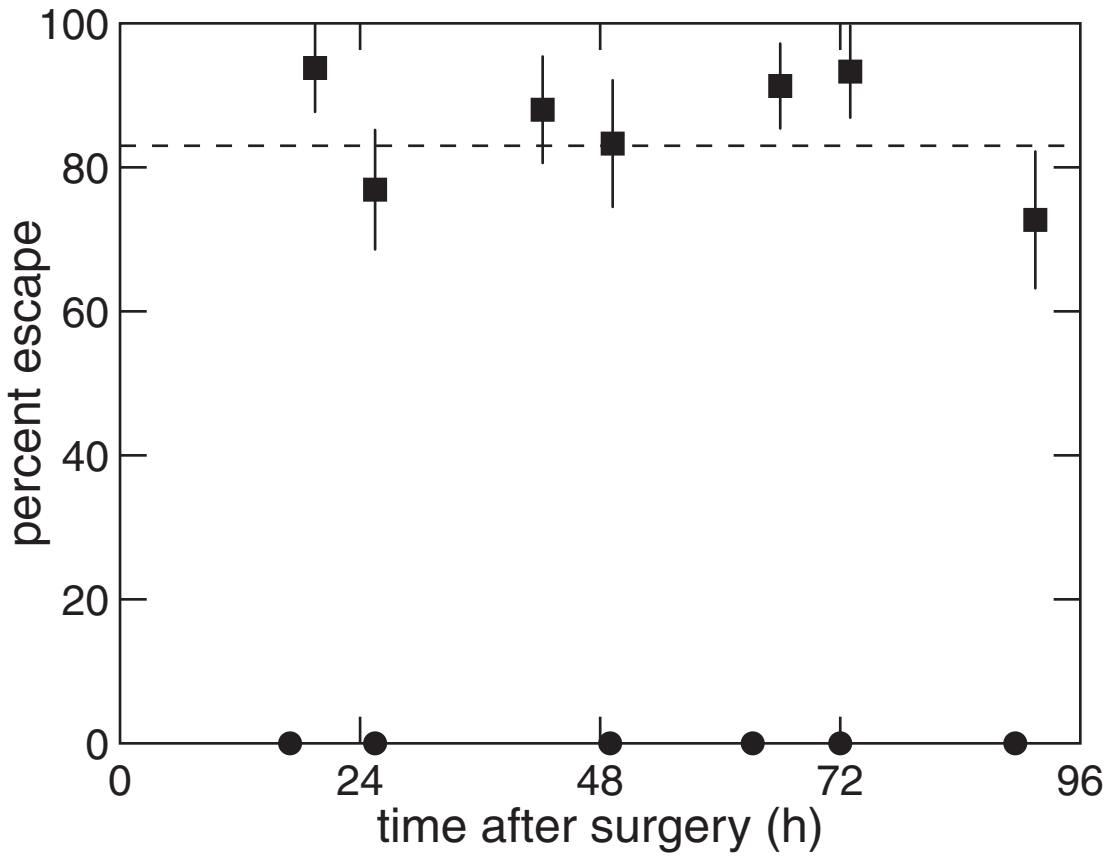
Nanoneurosurgery

escape rate of ASH-lacking mutant

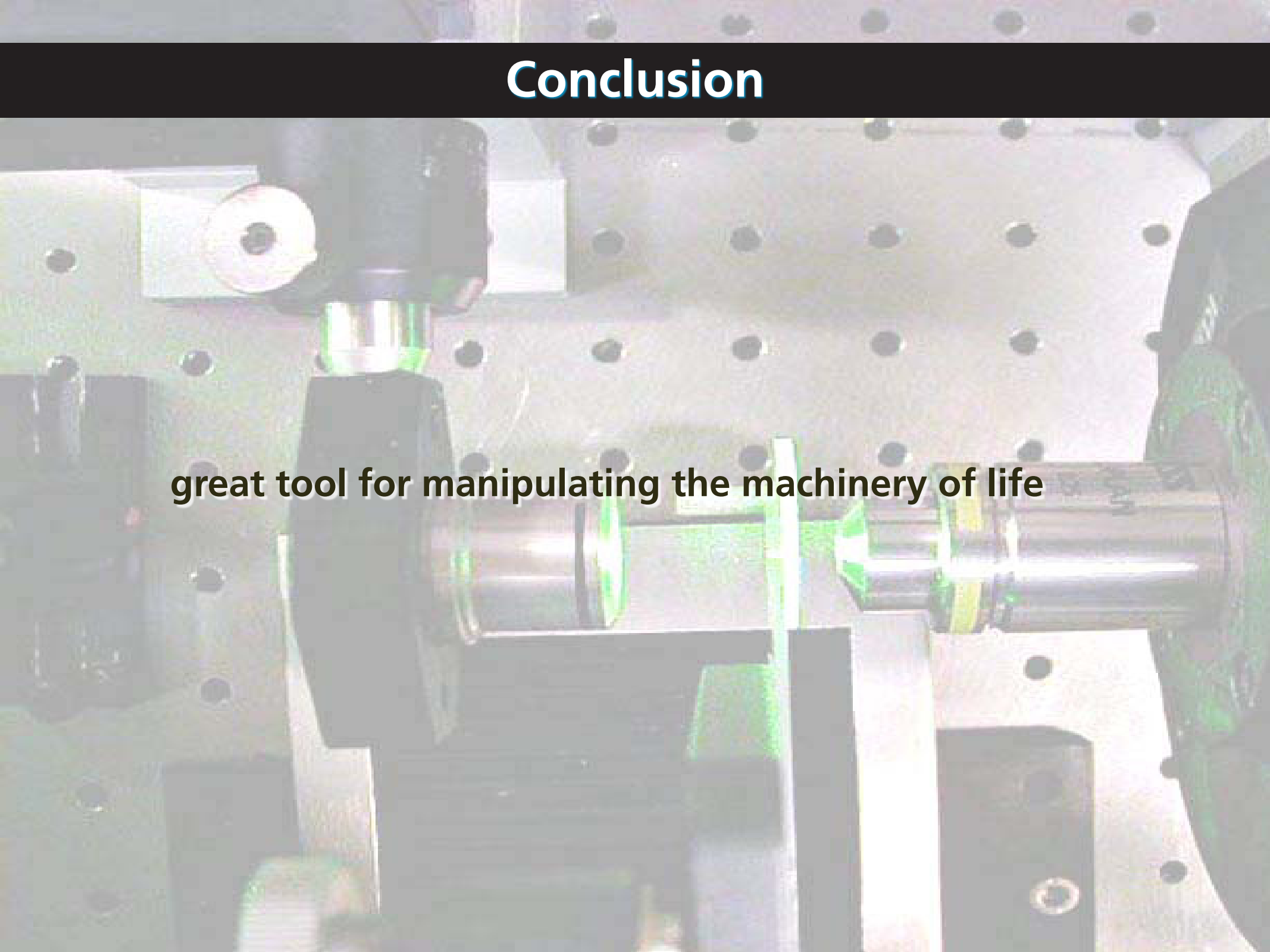


Nanoneurosurgery

escape rate after ASH-ablation surgery



Conclusion



great tool for manipulating the machinery of life

Funding:

National Science Foundation

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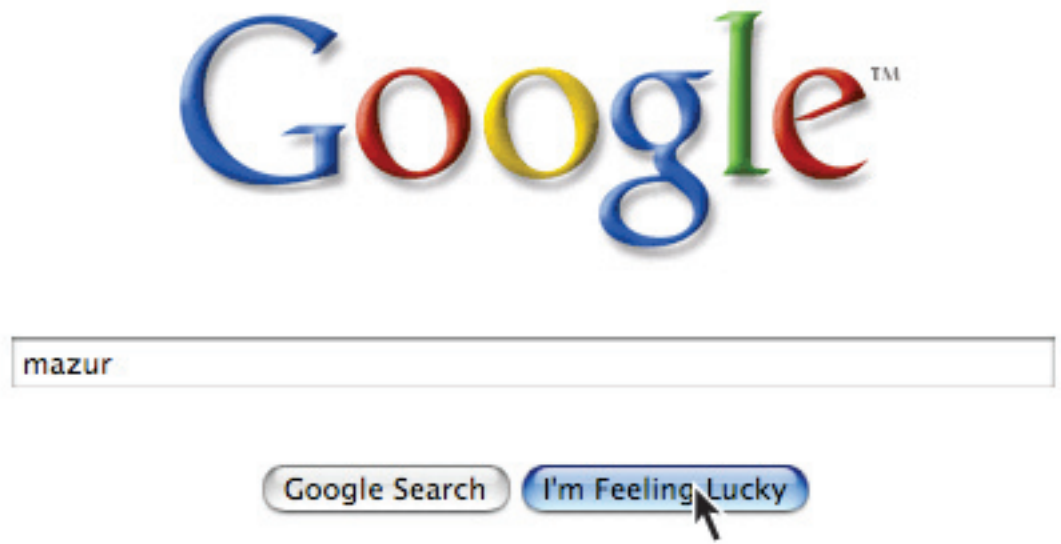
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