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Lecture: “Microrheology of a Complex Fluid” by Dr. Peter So.

Given August 10, 2006 during the GEM4 session at MIT in Cambridge, MA.

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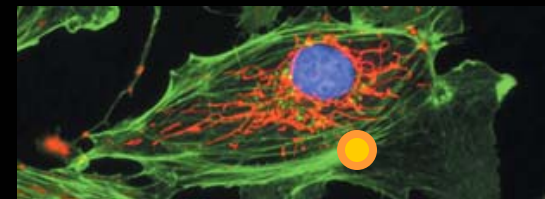
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Microrheology of Complex Fluid

- Rheology: Science of the deformation & flow of matter
- Microrheology
 - Microscopic scale samples
 - Micrometer lengths



Complex shear modulus $G^*(\omega)$

$$\sigma = G^* \varepsilon$$

- $G^*(\omega) = G'(\omega) + j G''(\omega)$
- Solid vs. fluid
- Resistance to deformation

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Storage modulus G'
 Energy storage
 Elasticity ~ Solid

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Loss modulus G''
 Energy dissipation
 Viscosity ~ Fluid

High Frequency Microrheology Measurement

Active Method:

Magnetic microrheometer – Baush, BJ 1998

Huang, BJ 2002

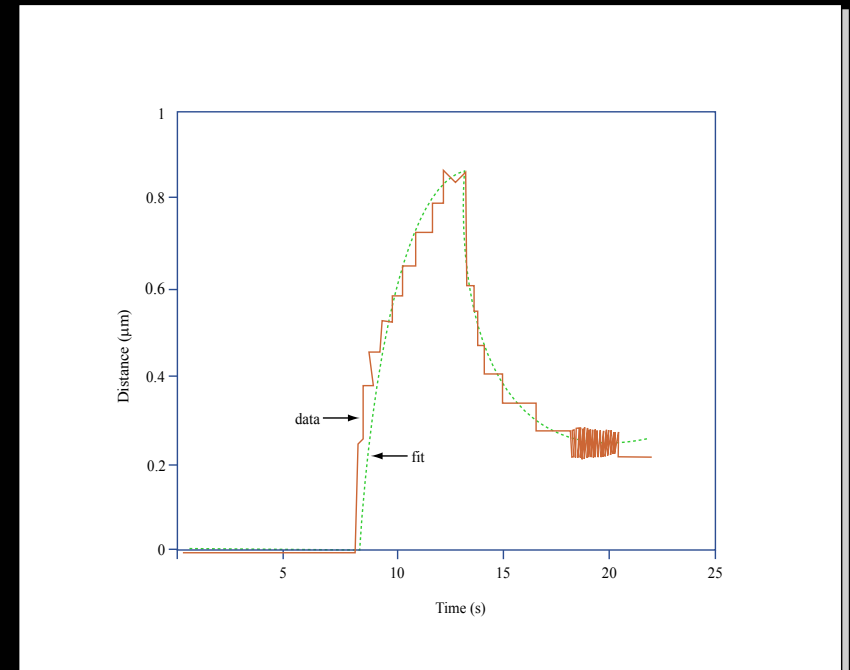
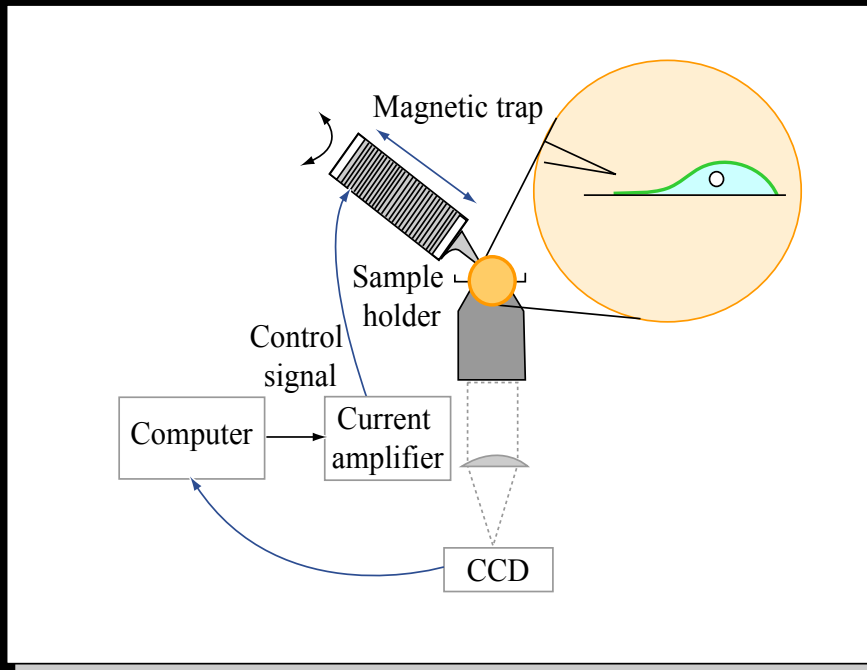
Passive Method:

Single particle tracking – Mason, PRL 1995

Yamada, BJ 2000

Multiple particle tracking – Crocker, PRL 2000

Magnetic Microrheology



Figures by MIT OCW.

Magnetic Microrheology

5 sec Step Response

Basic Physics of Magnetic Microrheometer



Ferromagnetic particle

$$\mathbf{F} = \frac{1}{2} \mu_0 \nabla (\mathbf{m} \cdot \mathbf{H})$$

Particles cluster together!
Doesn't work!

Paramagnetic particle – no permanent magnetic moment

$$\mathbf{F} = \mu_0 \chi V \nabla (\mathbf{H} \cdot \mathbf{H})$$

χ is susceptibility

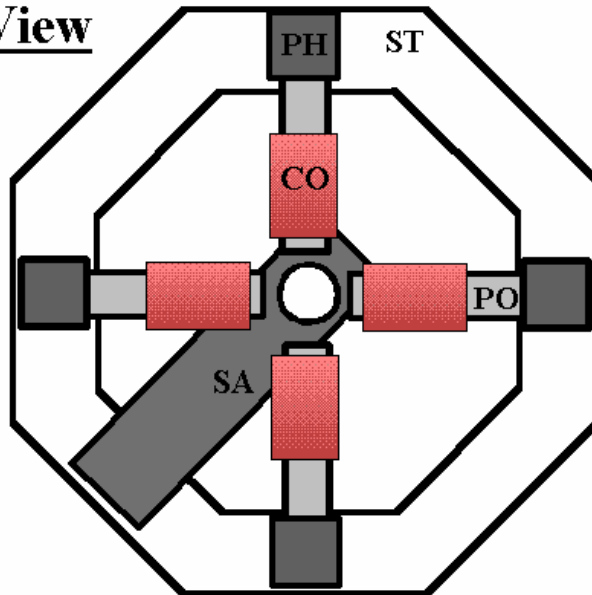
V is volume

Note: (1) force depends on volume of particle
(5 micron bead provide 125x more force)
(2) force depends on magnetic field GRADIENT

Magnetic manipulation in 3D

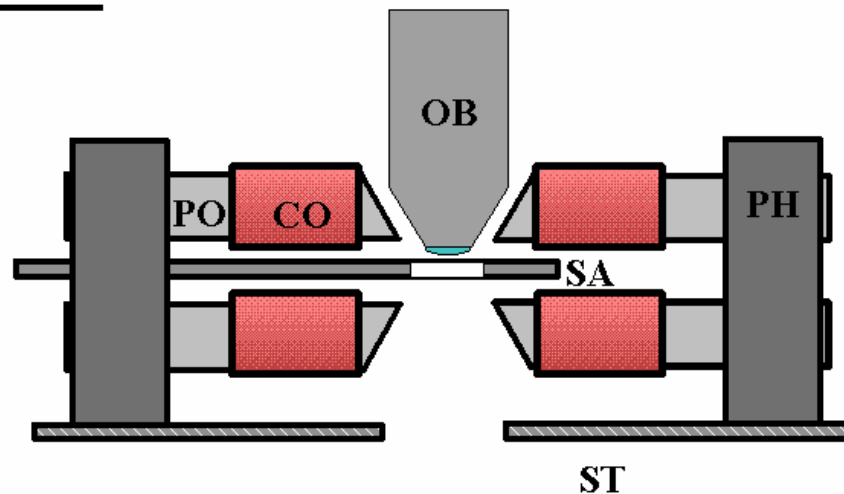


Top View



ST: stage
PH: post holder
CO: coil
(400 turn/cm)
PO: pole
SA: sample chamber
OB: objectives
(100x, 1.0 n.a.
water;
20x, 0.5 n.a
all reflecting)

Side View



*Lower Force
nN level

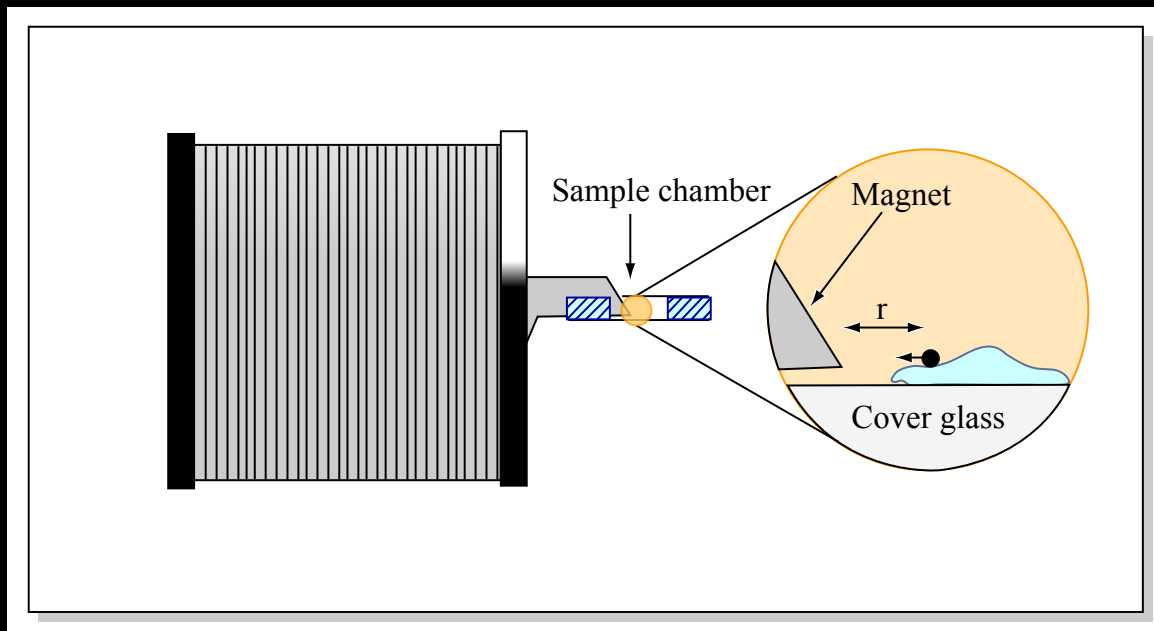
*3D

*Uniform gradient

Amblad, RSI 1996
Huang, BJ 2002

Courtesy of Dr. Peter So. Used with permission.

Magnetic manipulation in 1D



*High force
>10 nN

*Field non-uniform
Needs careful
alignment of tip
to within microns

*1D

Figure by MIT OCW. After Bausch et al., 1998.

The bandwidth of ALL magnetic microrheometer is limited by the inductance of the electromagnet to about kiloHertz

Magnetic Rheometer Requires Calibration

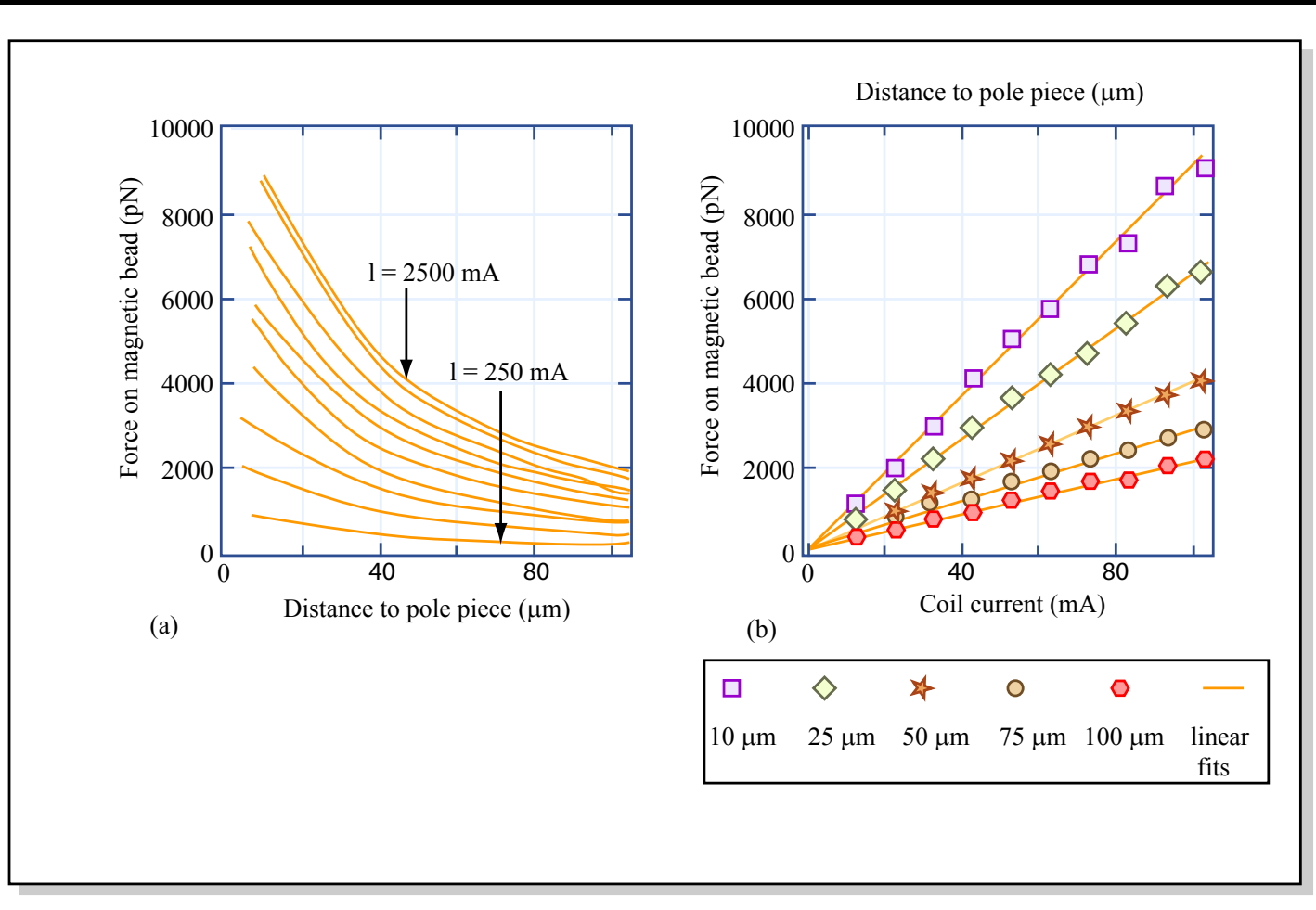


Figure by MIT OCW. After Bausch, 1998.

Mag Rheometer Experimental Results

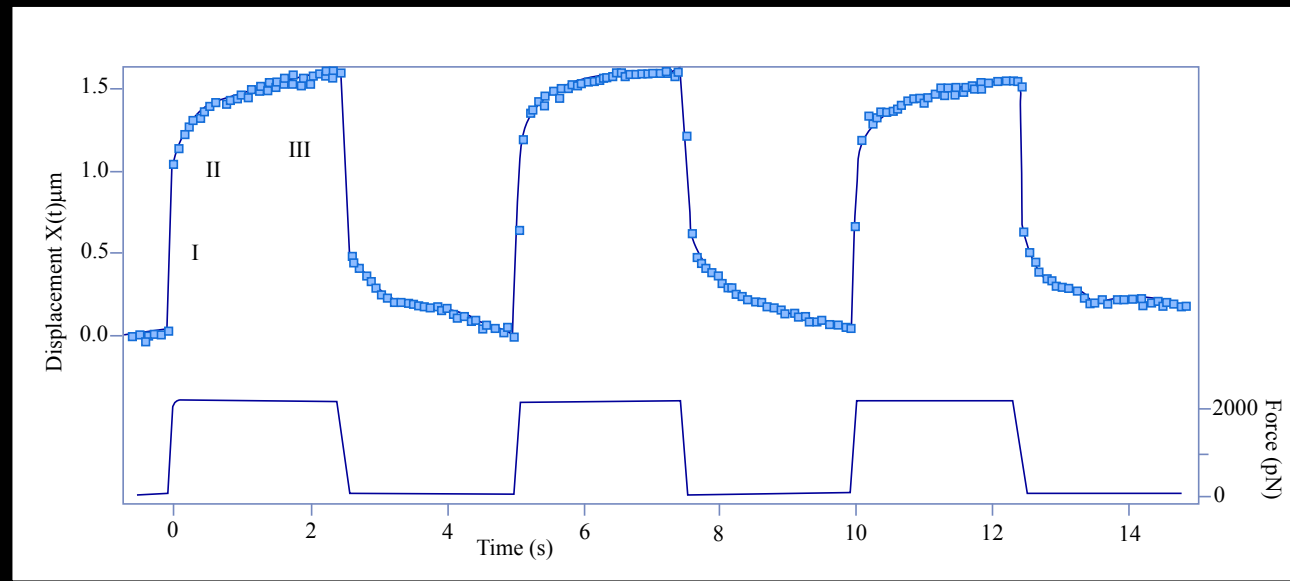


Figure by MIT OCW. After Bausch, 1998.

Transient responses allow fitting to micro-mechanical model

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See Fig. 5 in Bausch et al. "Local Measurements of Viscoelastic Parameters of Adherent Cell Surfaces by Magnetic Bead Microrheometry." *Biophys J* 75 (1998): 2038-2049.

Problem – Magnetic bead rolling

Solution – Injection, Endocytosis Modeling (Karcher BJ 2003)

Model Strain Field Distribution



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See Fig. 9 in Bausch et al. "Local Measurements of Viscoelastic Parameters of Adherent Cell Surfaces by Magnetic Bead Microrheometry." *Biophys J* 75 (1998): 2038-2049.

Single Particle Tracking



Consider the thermal driven motion of a sphere in a complex fluid

Langevin Equation

$$m\dot{v}(t) = f(t) + \int_0^t \xi(t-t')v(t')dt'$$

Inertial
force

Random
thermal
force

Memory function—
Material viscosity
Particle shape

Langevin Equation in Frequency Domain



Laplace transform of Langevin Equation

$$\tilde{v}(s) = \frac{\tilde{f}(s) + mv(0)}{\tilde{\xi}(s) + ms}$$

Multiple by $v(0)$,
taking a time average,
Ignoring inertial term

$$\tilde{G}(s) = \frac{kT}{\pi a s \langle \Delta \tilde{r}^2(s) \rangle}$$

Random force
 $\langle \tilde{f}(s)v(0) \rangle = 0$

Equipartition of energy
 $m \langle v(0)v(0) \rangle = kT$

Generalized Stokes Einstein
 $\xi(s) = 6\pi a \tilde{\eta}(s) \quad \tilde{G}(s) = s \tilde{\eta}(s)$

Definition and Laplace transform
of mean square displacement

$$\langle v(0)\tilde{v}(s) \rangle = s^2 \langle \Delta \tilde{r}^2(s) \rangle / 6$$

(2) Fluorescence Laser Tracking Microrheometer



- Approach: Monitoring the Brownian dynamics of particles embedded in a viscoelastic material to probe its frequency-dependent rheology

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mean squared displacement

$$\langle \Delta R^2(\tau) \rangle = \langle (\vec{r}(t+\tau) - \vec{r}(t))^2 \rangle$$



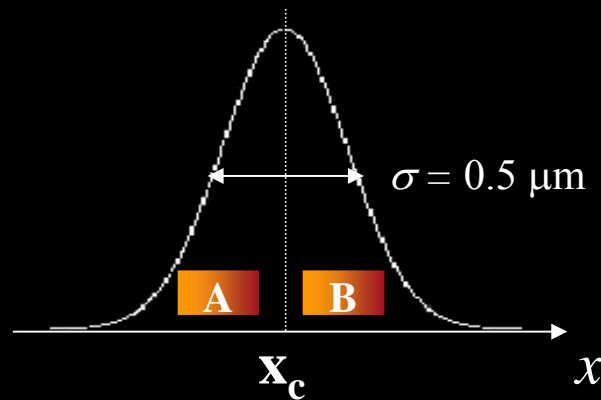
shear modulus

$$G^*(i\omega) = \frac{2k_B T}{3\pi \cdot a \cdot i\omega \cdot \langle \Delta \tilde{R}^2(i\omega) \rangle}$$

Yamada, Wirtz, Kuo, *Biophys. J.* 2000

(2) Nanometer Resolution for the Bead's Trajectory

- Collecting enough light from a fluorescent bead is critical



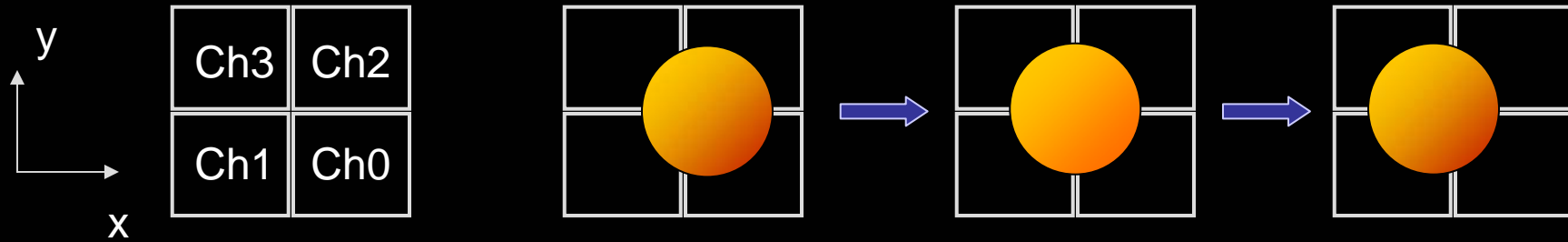
$$p(x) = \frac{1}{\sigma\sqrt{2\pi}} \exp\left[-\frac{(x-x_c)^2}{2\sigma^2}\right]$$

$$\frac{N_A}{N_B} = \frac{p(A)}{p(B)} = \frac{\int_{-\infty}^{x_c} \exp\left(\frac{-x^2}{2\sigma^2}\right) dx}{\int_{x_c}^{+\infty} \exp\left(\frac{-x^2}{2\sigma^2}\right) dx}$$

Photons detected per measurement	10^3	10^4	10^5	10^6
Uncertainty on $\frac{N_A}{N_B}$	0.033	0.010	0.003	0.001
Uncertainty on x_c (nm)	12	4	1.2	0.4

Nanometer resolution $\leftrightarrow 10^4$ photons per measurement

(2) Calibrating the FLTM



- 5-nm stepping at 5 or 50 kHz
- Curve fitting matches theory

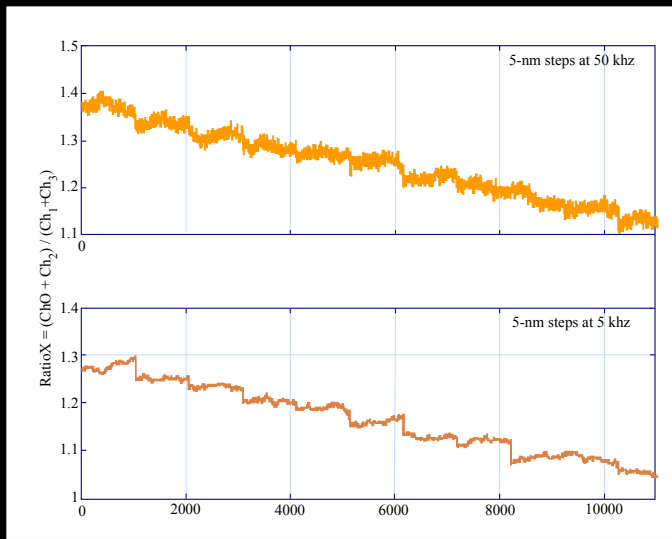


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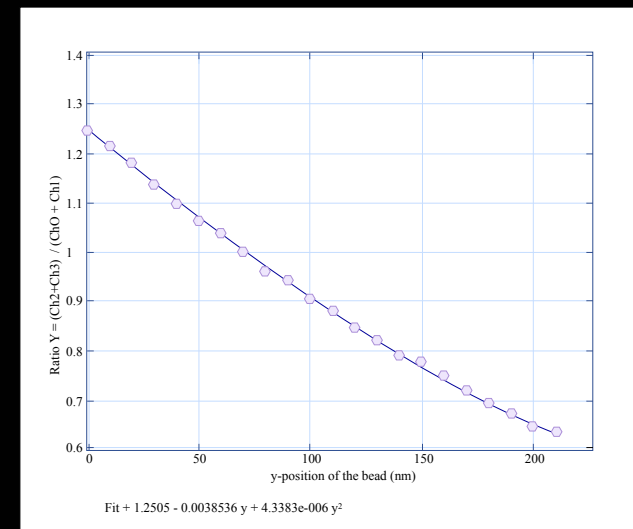


Figure by MIT OCW.

Characterizing the FLTM



- Using polyacrylamide gels (w/v 2% to 5%) of known properties
- ✓ Good agreement with previously published data

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See. Fig. 11(a) in Schnurr, B., F. Gittes, F. C. MacKintosh, and C. F. Schmidt.
"Determining Microscopic Viscoelasticity in Flexible and Semiflexible Polymer
Networks from Thermal Fluctuations." *Macromolecules* 30 (1997): 7781-7792.

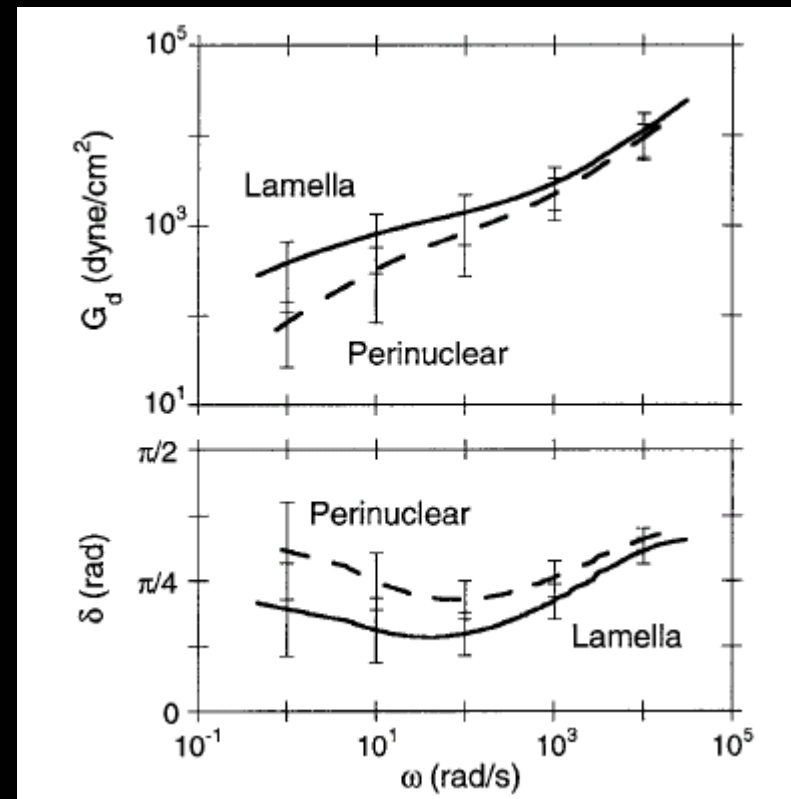
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Single Particle Tracking Data



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See Fig. 4(a) and 7 in Yamada, Soichiro, Denis Wirtz, and Scot C. Kuo. "Mechanics of Living Cells Measured by Laser Tracking Microrheology." *Biophys J* 78 (2000): 1736-1747.



Two- and Multiple Particle Tracking



SPT responses can be influenced by local processes (adhesion, active, etc) and do not represent global cytoskeleton behavior

Solution: Look at the correlated motion of two particles under thermal force

$$D_{rr}(r, \tau) = \langle \Delta r_r^i(t, \tau) \Delta r_r^j(t, \tau) \delta(r - R^{ij}(t)) \rangle_{i \neq j, t}$$

$$D_{rr}(r, s) = \frac{kT}{2\pi r s \tilde{G}(s)}$$

The major difference is that the correlation signal is a function of “r” the separation of the particles but not their size

Instead of using fast quadrant detectors, multiple particle tracking uses a wide field camera which is slower

SPT vs MPT

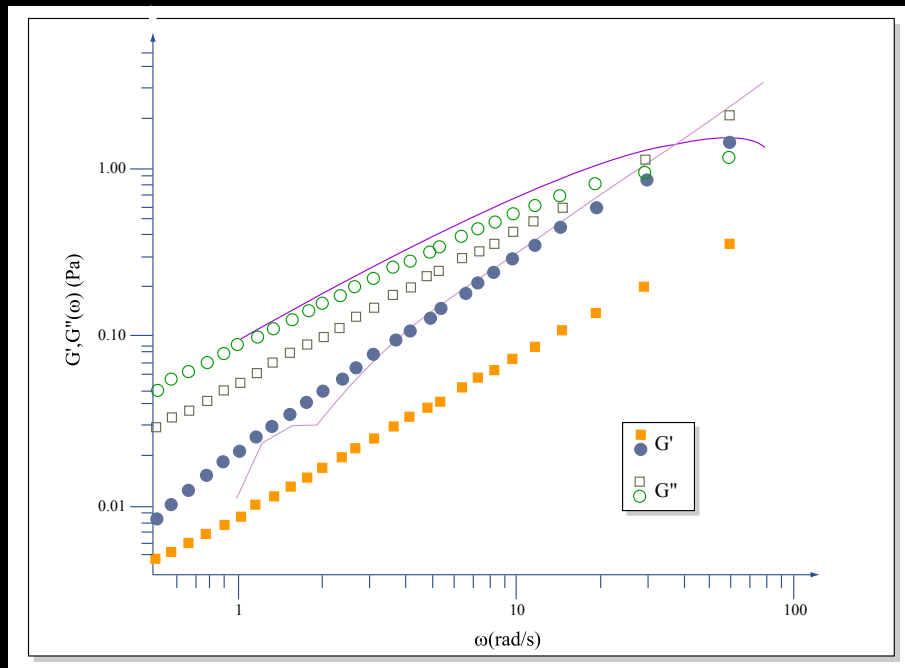


Figure by MIT OCW. After Crocker, 2000.

Triangle: SPT

Circle: MPT

SPT and MPT results can be quite different specially in cells

A Comparison of Microrheometry Methods



	Magnetic	SPT	MPT
Bandwidth	kHz	MHz	kHz
Signal Amplitude	μm	nm	nm
Local Effects	Yes	Yes	No
Nonlinear regime	Yes	No	No
Instrument	Intermediate	Intermediate	Simple