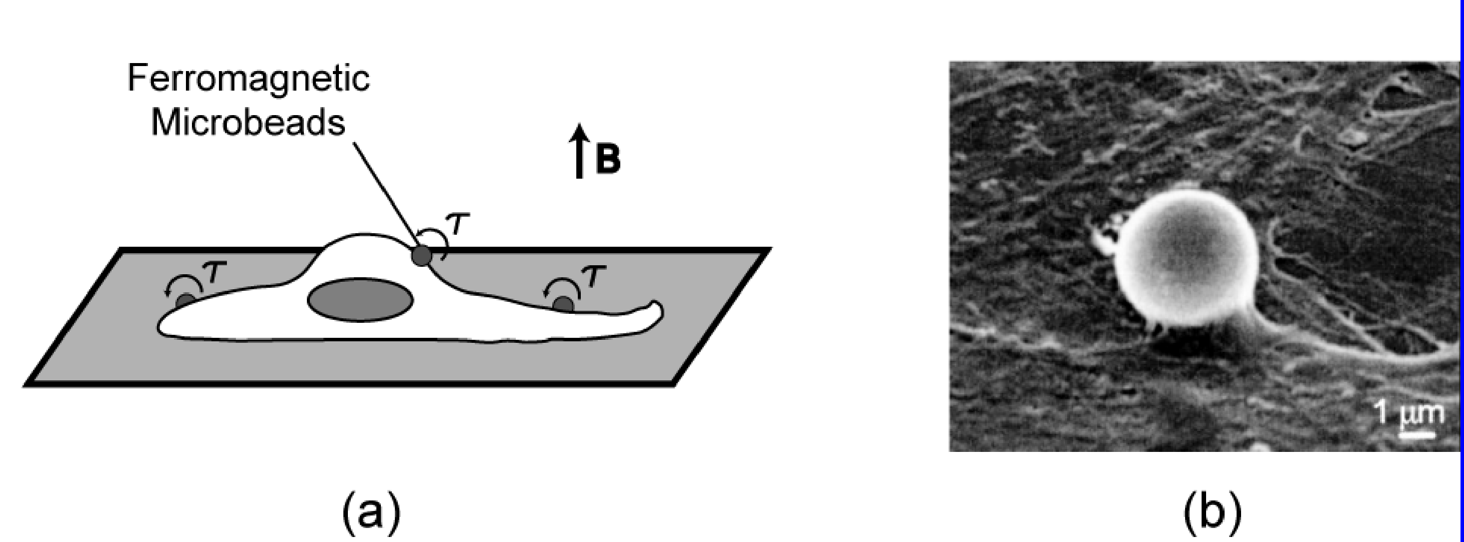
Session 17

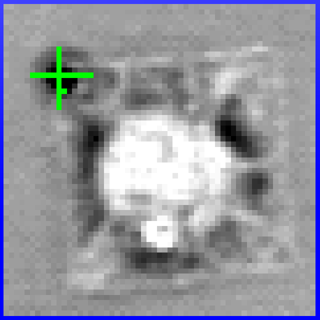
SOFT GLASSY RHEOLOGY

Recall: Magnetic Twisting Cytometry

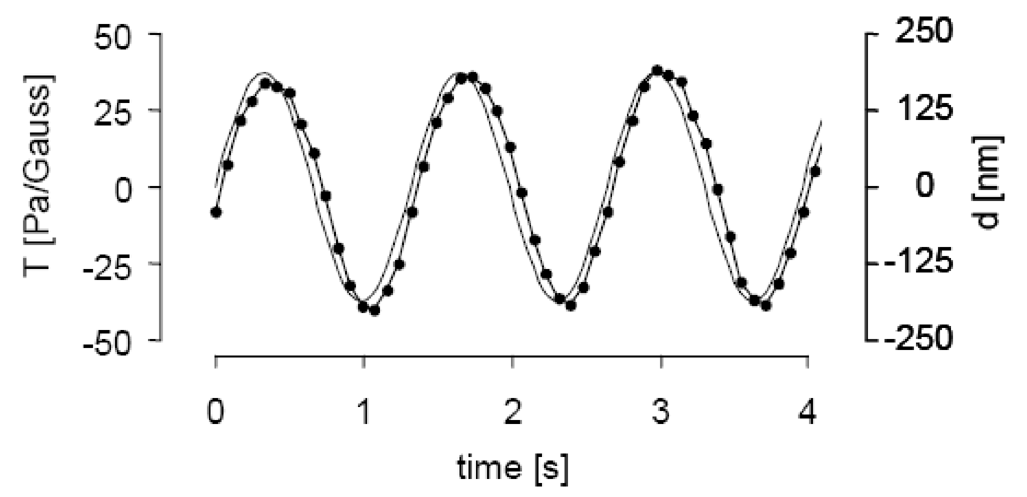
- Torque applied at surface of cells with magbeads
- Used to determine cell mechanics
  - Cellular viscoelasticity (Fabry, Fredberg)
  - Mechanotransduction (Wang, Ingber)



Particle Tracking Measurement



- Fast, real-time image analysis
  - 16 frames per twist
  - Stroboscopic technique for >1 Hz twists
- Individual particle tracking using intensity-weighted centroid calculation.
- Small phase lag between twist frequency and displacement frequency



Complex Modulus

- Complex modulus defined by ratio of complex applied torque and complex bead displacement

$$\tilde{g} = \tilde{T} / \tilde{d}$$

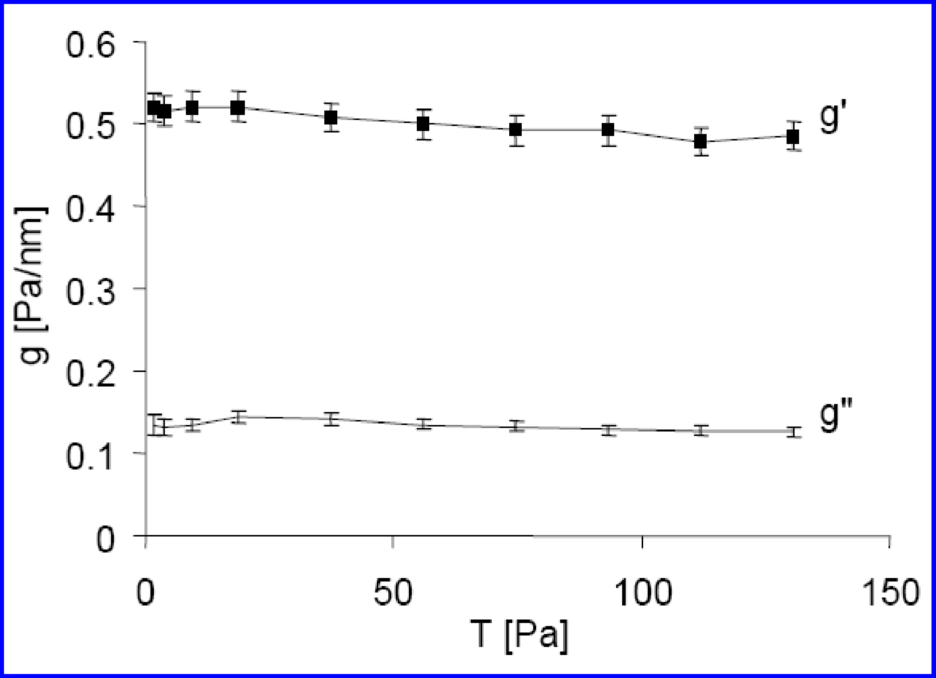
- Elastic (storage) modulus: $g' = \mathrm{Re}(\cdot)$
- Loss modulus: $g'' = \mathrm{Im}(\cdot)$
- Loss tangent: $\eta = g''/g'$

- Transform to storage modulus and loss modulus through geometric factor α = 6.8 µm

$$\tilde{G} = \alpha \tilde{g}$$

Shear Stress Response

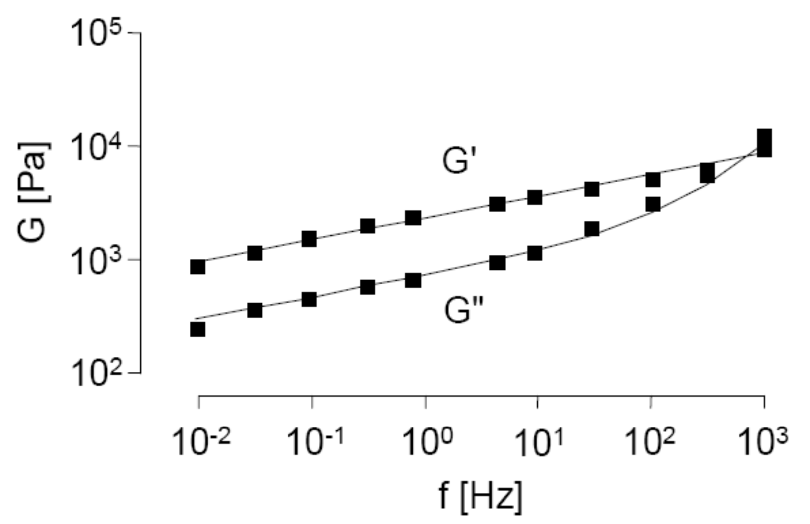
- Physiological range of stress
- Linear mechanical behavior observed
- No observation of nonlinear behavior as by others
  - Strain-hardening
  - Shear-thinning



Frequency Response

- Storage modulus
  - Increased with frequency
  - Weak power law observed on log-log plot

$$G' \simeq f^{x-1}$$



- Loss modulus
  - Smaller than G′ except at 1 kHz
  - Weak power law observed for < 10 Hz
  - Newton viscosity characteristics observed > 10 Hz
    - Slope approaches 1 (x = 2)

Structural Damping Law

- In angular frequency domain ($\omega = 2\pi f$)

$$\tilde{g} = g_0 \left(\frac{\omega}{\Phi_0} \right)^{x-1} \left(1 - i\bar{\eta}\right) \Gamma\left(2 - x\right) \cos\frac{\pi}{2}\left(x - 1\right) + i\omega\mu$$

$$\bar{\eta} = \tan\frac{\pi}{2}\left(x - 1\right)$$

  - Scale factor for stiffness: g_0
  - Scale factor for frequency: Φ_0
  - Gamma Function: Γ
  - Newtonian viscosity: μ

Structural Damping Law

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- Storage modulus is real part of equation
- Loss modulus is imaginary part of equation
  - Newton viscous term $i\omega\mu$ relevant at hi frequency only
  - As $x \rightarrow 1$, slope (x-1) $\rightarrow 0$, $\bar{\eta} \rightarrow 0$, $g' \rightarrow g_0$ (Solid-like)
  - As $x \rightarrow 2$, cos(·) $\rightarrow 0$, $\bar{\eta} \rightarrow \infty$, $g'' \rightarrow \mu$ (Fluid-like)

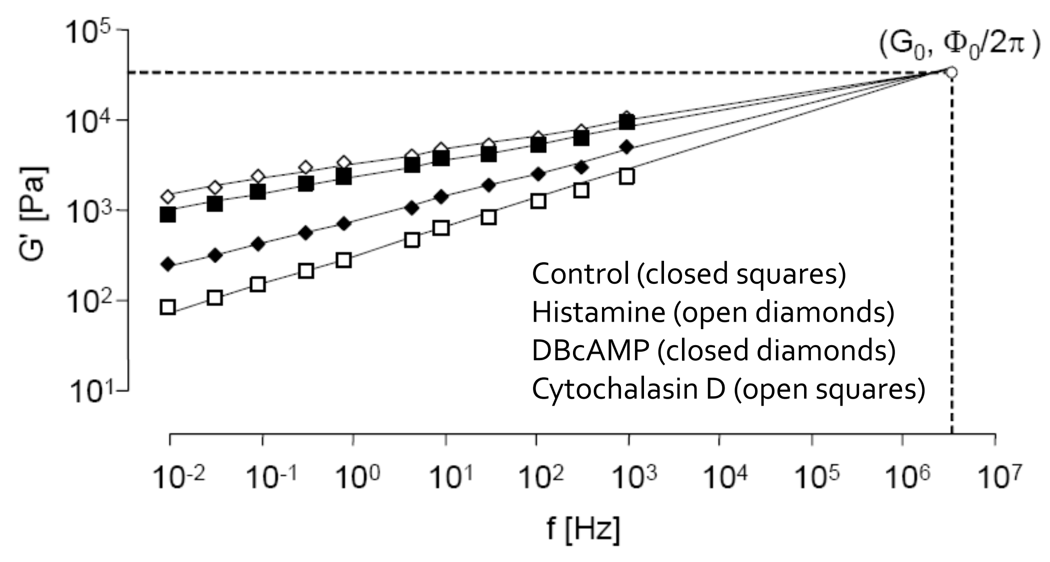
Independence of Parameters

- Structural damping described by parameters:
  - Scale factor for stiffness: g_0
  - Scale factor for frequency: Φ_0
  - Newtonian viscosity: μ
  - Power law exponent: x

- Noise temperature (x) is master parameter
  - Shown in following slides

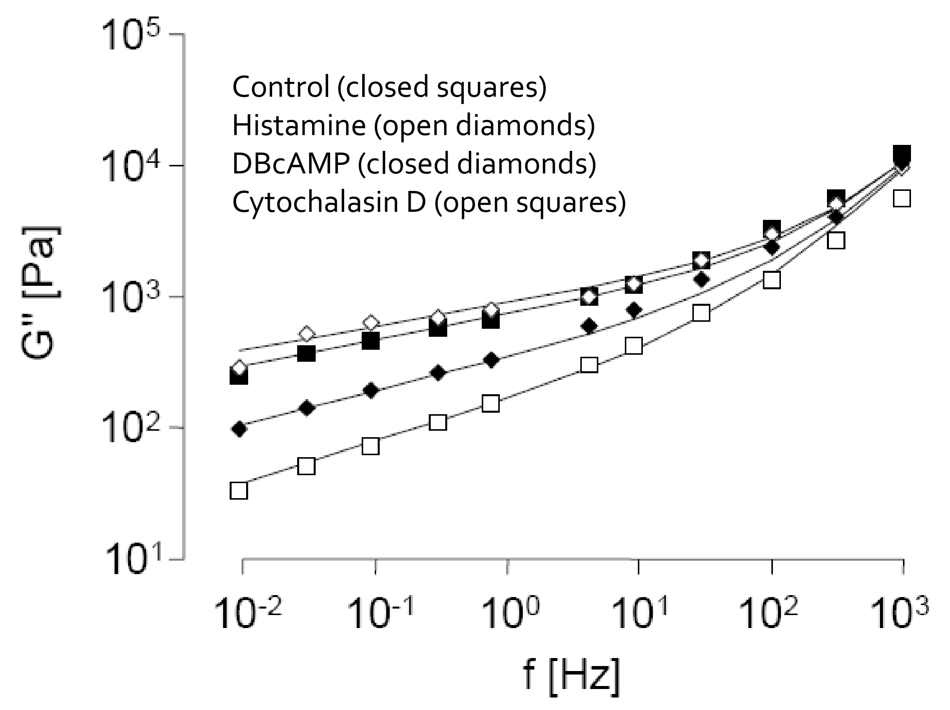
Contractility & CSK Disruption

- Common intersection exists for G′ vs. *f* curves
  - Lines represent structural damping equation
  - Parameters g_0, Φ_0 appear invariant with drugs
- Statistical analysis
  - 3 parameter fit (g_0, Φ_0, x) is not statistically different than 1 parameter fit (x and g_0, Φ_0 fixed)



Contractility & CSK Disruption

- Loss moduli merge onto single curve at high f
- Fixed μ can match the data
- However, varied μ can slightly improve statistical fit
- This plus g_0, Φ_0 argument indicates x as single cell mechanics parameter

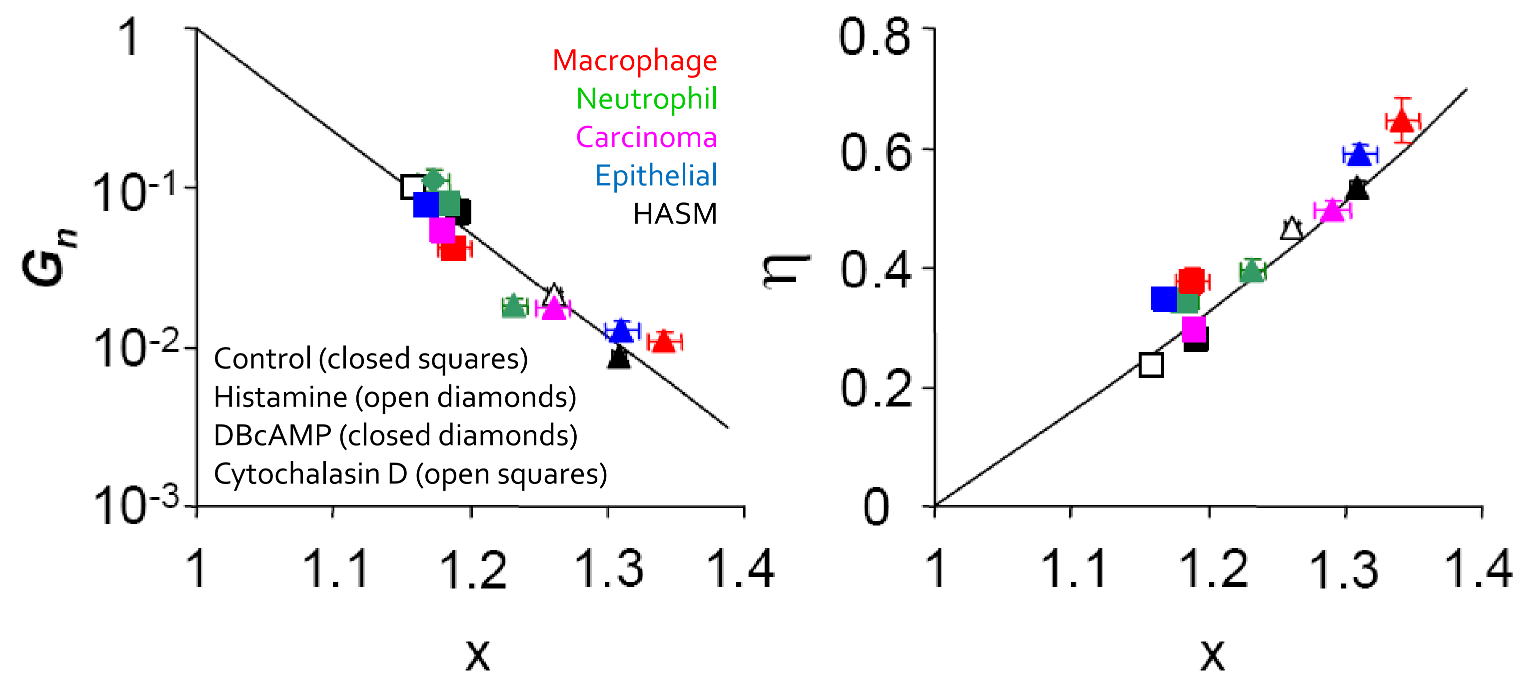


Universality

- Common structural damping behavior
  - Power-law for G′ and G″ vs. f
  - Common extrapolated intersection of G′ vs. f with drug treatment
  - Merging of G″ vs. f curves to single line at high freq
- Observed in
  - Cell types: macrophages, neutrophils, endothelial, epithelial, fibroblasts, cancer cells
  - CSK drugs: Myosin inhibitors (BDM), MLCK inhibitors (ML-7, ML-9), ROCK inhibitors, actin polymerizing inhibitors (Latrunculin), actin stabilizers (jasplakinolide)
  - Ligand types: RGD-peptide, collagen, vitronectin, fibronectin, urokinase, acetylated-LDL, adhesion receptor antibodies
  - Testing systems: AFM, mag-tweezers, rotating disk rheometers

Master Curves

- Normalized stiffness $G_n = G'_{0.75\ \mathrm{Hz}} / G_0$



$$G_n = \frac{G'}{G_0} = \frac{\mathrm{Re}\left(\tilde{G}\right)}{G_0} \Rightarrow \ln G_n = (x-1)\ln\left(\frac{2\pi f}{\Phi_0}\right) \qquad \eta = \tan\frac{\pi}{2}(x-1)$$

Soft Glassy Rheology

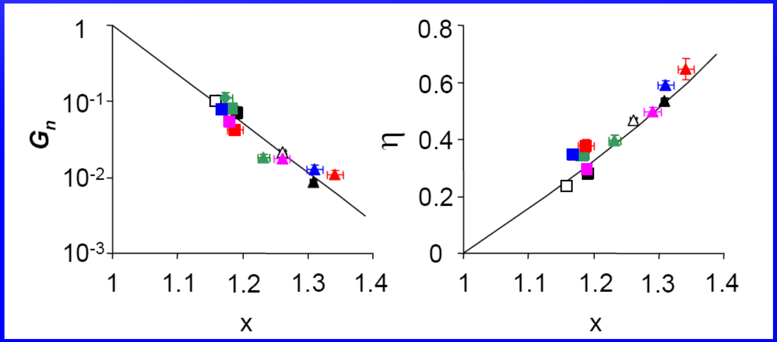
- Material types include foams, pastes, colloids, emulsions, slurries, (and cells)
- Common behavior
  - Small elasticity (Pa to 1 kPa)
  - Weak power-law for G′ and G″ vs. *f*
  - Loss tangent η is frequency independent and order 0.1
- Shared generic properties
  - Composed of elements that are discrete, numerous, aggregate with one another via weak interactions
  - Geometric arrangement that is structurally disordered and metastable

Soft Glassy Rheology Theory

- Elements (particles, proteins, beads, etc.) contained in an energy landscape that contains deep energy wells
  - Energy wells defined from interactions with other elements
  - Individual elements unable to escape wells by thermal energy alone but by agitation
- Parameter x is measure of agitation
  - "Effective Temperature" or "Noise Level"
  - When $x = 1$, materials is in a frozen state has ordered structure and elasticity
  - When $x > 1$, sufficient "noise" that elements can hop between wells. and system can flow and become more disordered

Soft Glass Rheology for Cells

- Cellular energy wells from CSK binding energies
  - Actin filament cross-linking
  - Actin-myosin cross-bridges
  - Hydrophobic interactions
  - Ionic charge or size exclusion



- Drug effects
  - Agents that inactivate contractile apparatus or cytoskeletal disruption move cell away from frozen state (glass transition)
  - Decreasing noise temperature is formation of ordered structure
  - Increasing noise temperature is disordered and fluid state