Using Atomic Force Microscopy to Quantify Cell Viscoelasticity

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Mechanosensing: What we know and what we really don’t

KNOWN:
• Cells respond to mechanical properties of their environment
• Cytoskeletal restructuring
• Impacts biological processes

UNKNOWN:
• What is specifically being altered?
• How is this mechanical response taking place?
• How do we make sense of this change?

1Kollmannsberger et al. Soft Matter, 2011, 7, 3127-3132
2Mina Shojaei Zadeh
Mechanosensing: What we know and what we really don’t

This is important because:
• Provides information to technologies that rely on cellular processes
• Stepping stone in modeling of mechanotransduction pathway
• Mechanophenotyping for cell targeting and classification

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We Examined…

Substrate Stiffness

- Increase understanding of the effect of the extracellular matrix
- Collagen-coated gels of varying concentrations of acrylamide/bisacrylamide

Compromised Cytoskeleton

A Combination of the Two

- Does the effect of intermediate filament expression change as a function of substrate stiffness?

Tang et al, 2008
Viscoelasticity and the Atomic Force Microscope

• Characterization of material that is neither completely viscous or completely elastic

Presentation and subsequent quantification of cell response

Chan et al., 2004
Quantifying Viscoelasticity

Taylor Expansion

\[ F_N = \frac{2}{\pi} \cdot \frac{E}{\left(1 - \nu^2\right)} \cdot \frac{\delta^2}{\tan \theta} \]

Elastic:

\[ E' = |E^*| \cdot \cos \psi \]

Viscous:

\[ E'' = |E^*| \cdot \sin \psi \]

Plan of Attack: Apply a sinusoidal stress function to cell surface

Picking the Parameters

- Position modulated versus force modulated
- Approach velocity
- Trigger point

Data Collection:
- 24x24 force maps for normal cells
- 3 force curves per vimentin null cell
Making the Data Mean Something

- Viscoelasticity causes exponential creep in data
  - Remove this with fitting lines to the natural log of data
What the Data Shows—Substrate Variation
What the Data Shows– Substrate Variation

N = 4
Vimentin Null Results

![Graph showing modulus values for normal and vimentin null fibroblasts.](image)

- Normal fibroblasts (N = 30 cells)
- Vimentin null fibroblasts (N = 20 cells)

* p < 0.04
Some Fine Tuning to Come…

- Increased robustness in reducing exponential creep
- Implement a second method for calculating $E''$

\[ \mu_{cell} = E_r * (\tau_\sigma - \tau_\varepsilon) \]

- Force curves spread across perinuclear region over full maps
- Examine vimentin null cells on substrates of varying stiffness

Conclusions

- Elastic modulus of the cells increases as a function of substrate stiffness, while loss tangent ($E''/E'$) decreases
- Vimentin null cells exhibit higher $E'$ and $E''$ values
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