

Adenocarcinoma cell mechanobiology is altered by the loss modulus of the surrounding extracellular matrix

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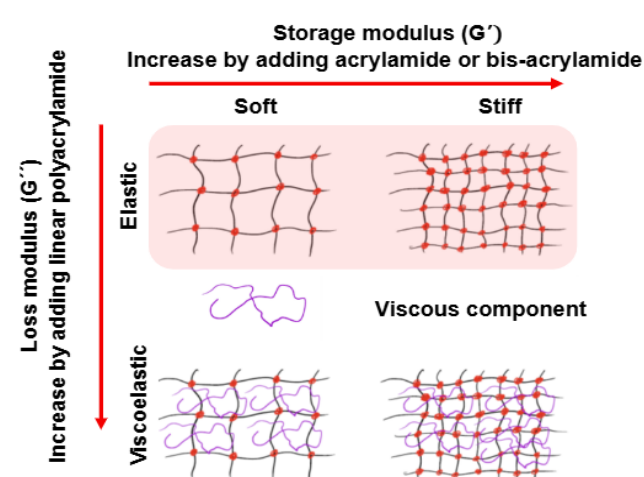
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Abstract

- Change in the elastic and viscoelastic ECM substrate affects several cellular processes such as morphogenesis, wound healing, and angiogenesis.
- Recently studies use viscoelastic hydrogels to mimic *in-vivo* mechanical environments.
- Based on several studies viscous dissipation of ECM regulates cell migration rate and elasticity regulates net contractility.¹⁻³

Methods

Fabrication and characterization of hydrogels

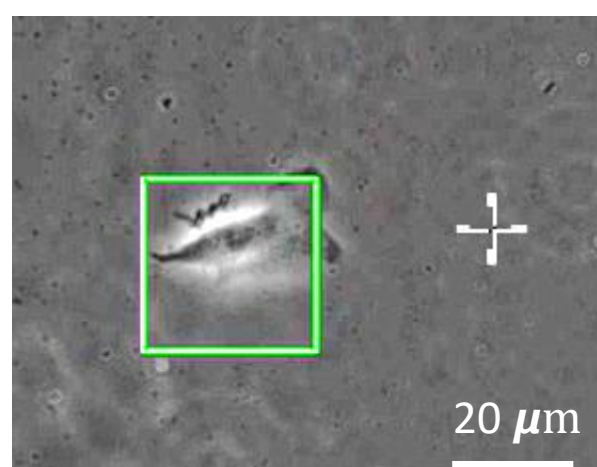


G' = Storage modulus (elastic component)
 G'' = Loss modulus (dissipative component)

- PAH can be tuned by changing the monomer (acrylamide) and crosslinker (bis-acrylamide) to obtain storage modulus (G') over a range of magnitudes.¹⁻⁴

By embedding linear PAA chains, it is possible to tune the loss modulus (G'')

Real-time quantification of cell parameters



From 24-hr timelapse:

- Alpha (behavior of the cell during migration)
 - Migration speed (how fast)
 - Projected cell area

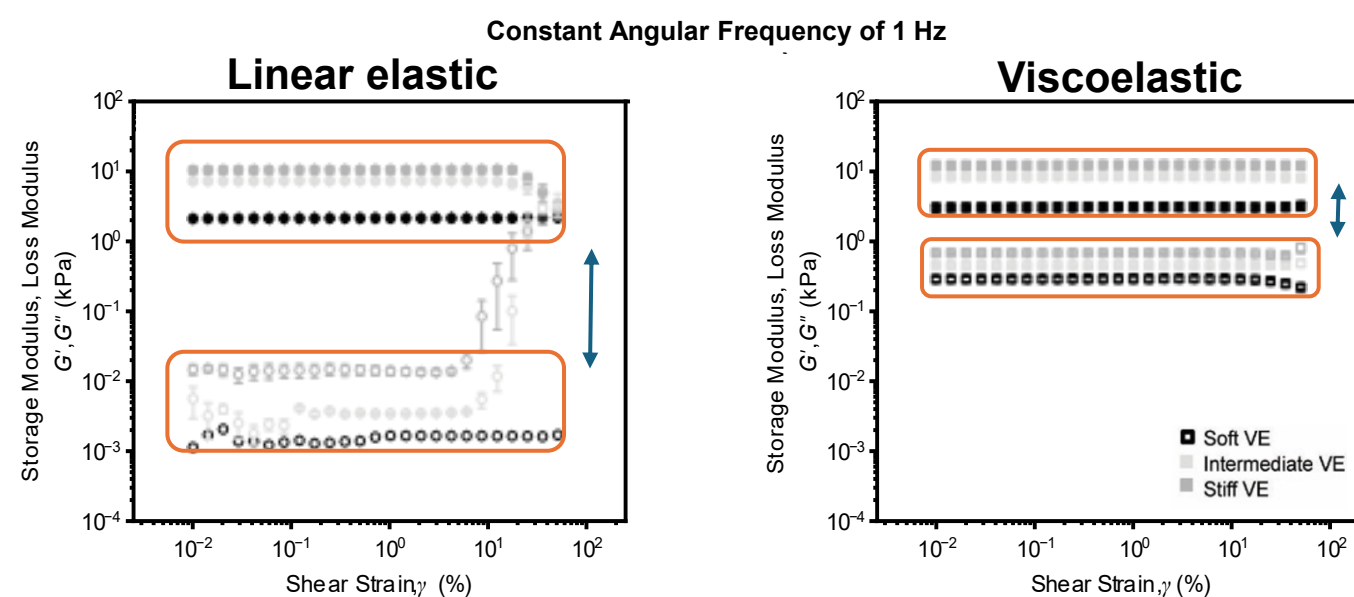
References

1. Smith A.M., et al., ACS Applied Polymer Materials, 2024
2. CM Lo et al., Biophysical Journal, 2000
3. Jamney et al., Nature, 2002
4. Tomasek et al., Nature, 2002



Results

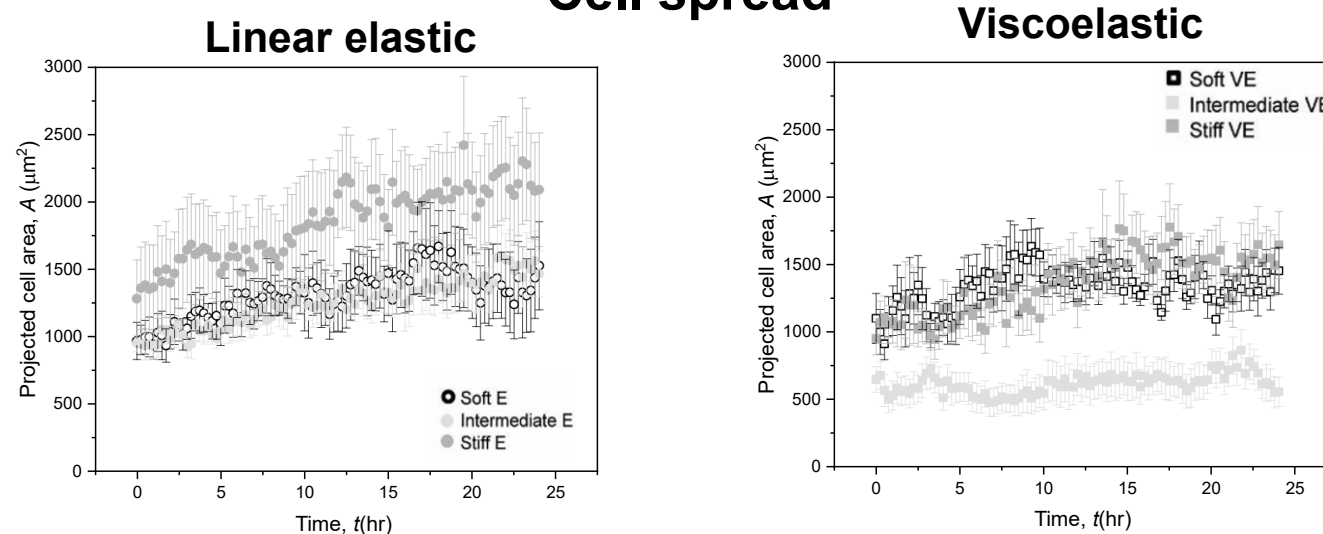
Rheology



Rheological properties as a function of shear strain at constant angular frequency of 6.28 rad/s (or 1 Hz). We show the storage modulus (G' , filled symbols) and loss modulus (G'' , open symbols) for model (left) elastic and (right) viscoelastic ECM.

An increase in loss modulus leads to viscoelastic ECM

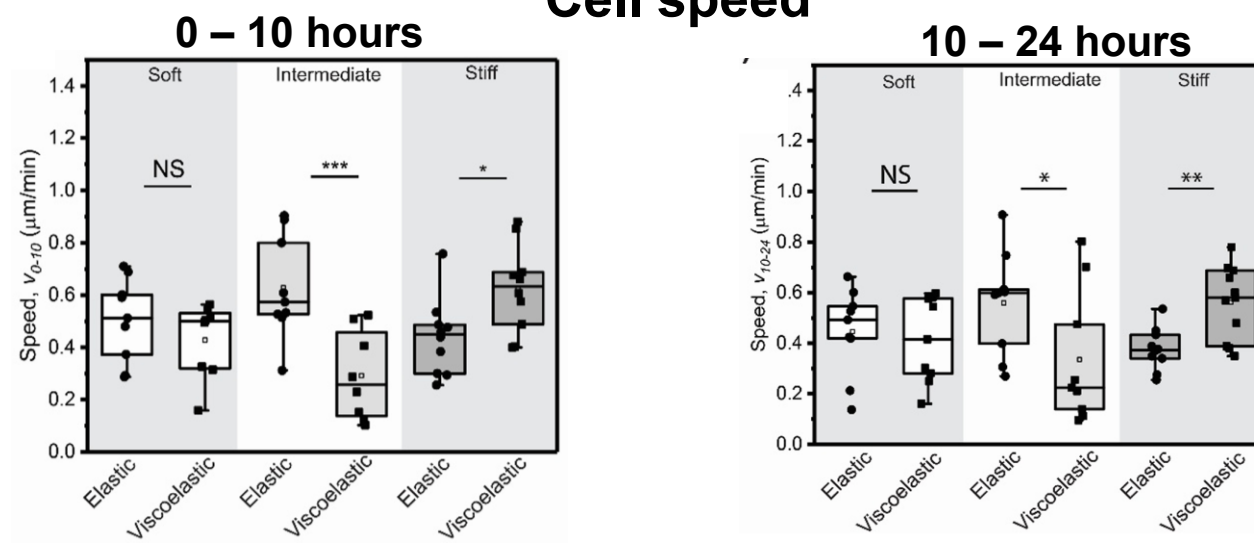
Cell spread



A549 cells projected cell area on soft, intermediate, and stiff elastic model ECMs over 24 hours, respectively (left). A549 cells projected cell area on soft, intermediate, and stiff viscoelastic model ECMs over 24 hours, respectively (right).

A549 showed differences in projected cell area on intermediate model ECMs

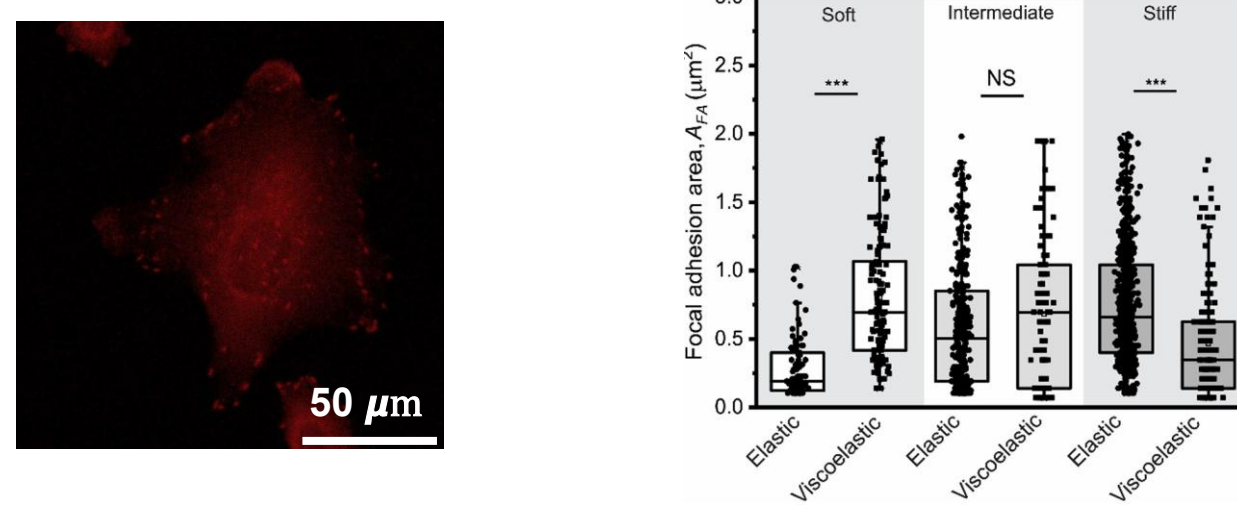
Cell speed



Cell area on soft, intermediate, and stiff elastic and viscoelastic model ECMs from 0 – 10 hours (left). Cell area on soft, intermediate, and stiff elastic and viscoelastic model ECMs after 10 hours (right).

A549 cells speed is similar on soft elastic and soft viscoelastic ECM, but not on stiff elastic and stiff viscoelastic

Focal adhesion



Immunofluorescence image of paxillin in A549 cells on stiff elastic model ECM (left). Focal adhesion area of A549 cells on soft, intermediate, and stiff elastic and viscoelastic model ECMs (right).

A549s displayed different FA area on soft and stiff model ECMs

Conclusion

- We introduce three ranges of stiffness (soft, intermediate, and stiff) with a tunable loss modulus for use as a model ECM.
- A549s on soft model ECMs cannot distinguish elasticity from viscoelasticity, but do distinguish on stiff elastic and stiff viscoelastic.