Reconfigurable Microenvironments Uncover Mechanosensing Timescales and Direct Cell Polarity

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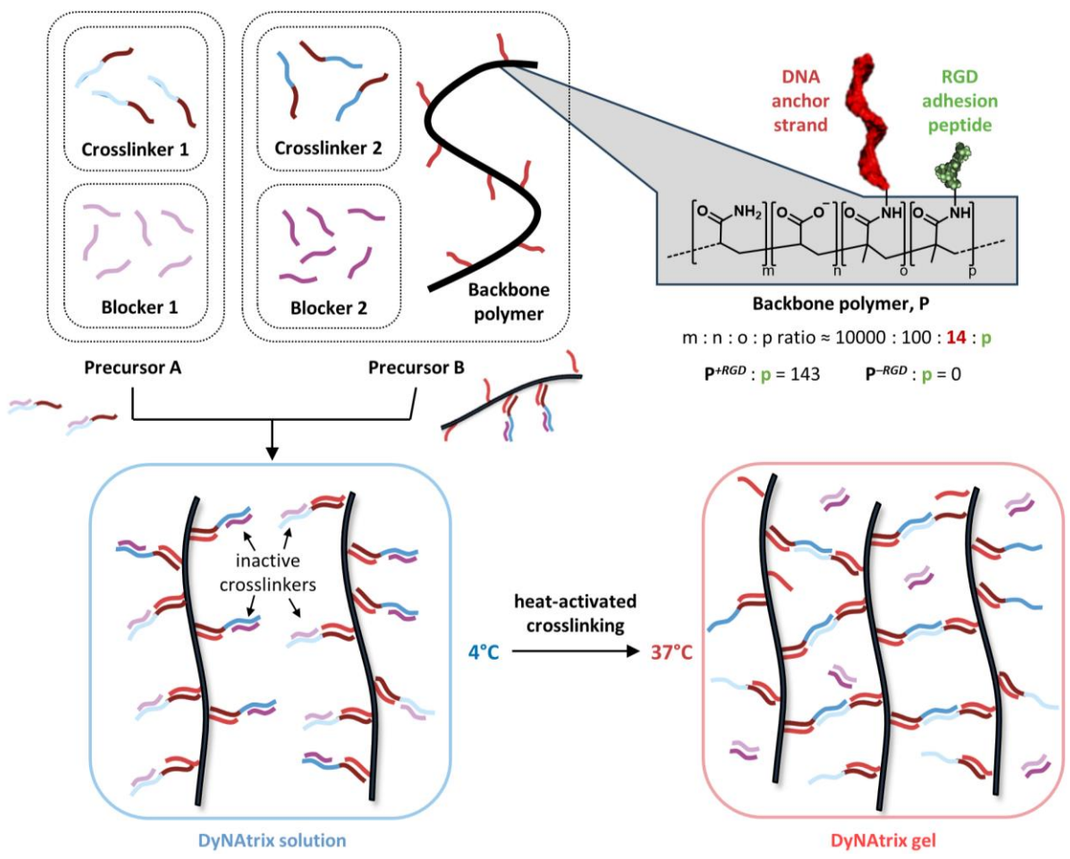
Abstract

In vitro tissue and disease modeling rely on matrices with tunable mechanical properties. Particularly, the polarity of cellular structures highly depends on the mechanical properties of the culture matrix. Nonetheless, currently available matrices often lack tunable viscoelasticity with user-defined control or require re-synthesis that largely alters the chemical composition. Here we demonstrate the dynamic control over viscoelasticity in a DNA-crosslinked hydrogel (DyNAtrix).[1,2] By analyzing MDCK cysts cultured in DyNAtrix, we correlate the apical-basal polarization with the surrounding mechanical properties. Finally, DNA nanotechnology[3] enables reversible switching of the stress-relaxation characteristic of DyNAtrix, which allows back-and-forth transformation of cell polarity. Altogether, this study highlights the application of DNA-based matrix engineering in programmable 3D cell culture, advancing the research on biomechanics, biophysics and tissue engineering.

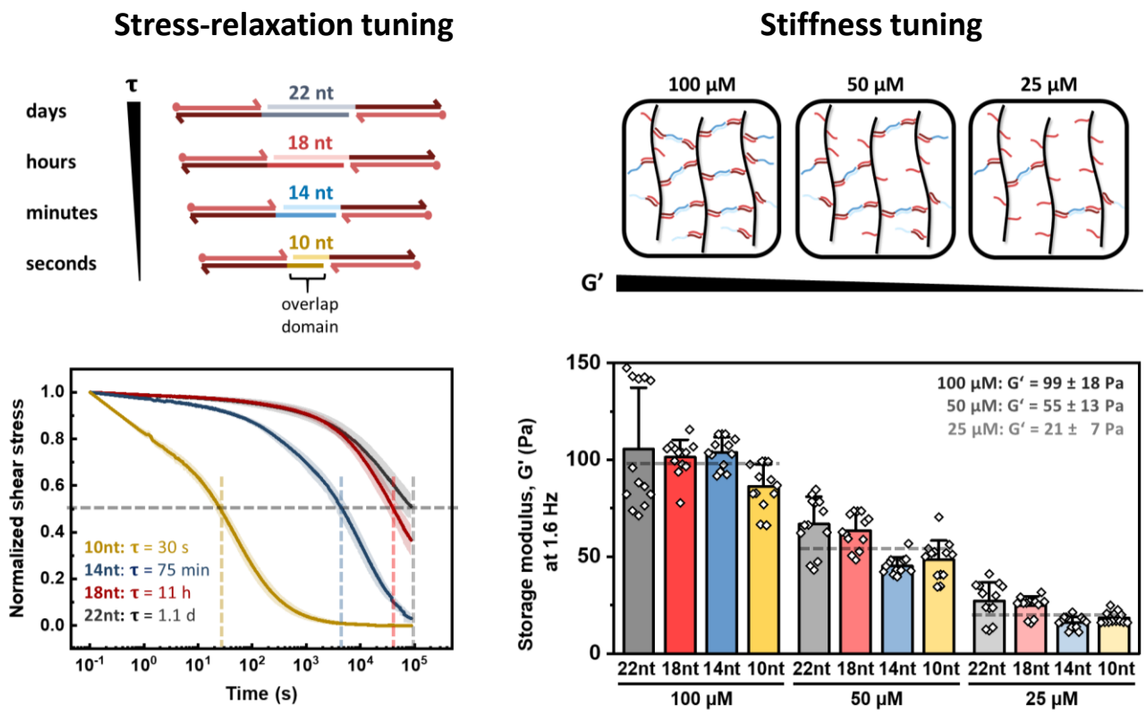
Results

Overview of DyNAtrix

- **DNA crosslinkers** enable mix-and-match gel formation.
- **Blocker DNA** allows tunable control of gelation kinetics.
- **RGD peptides** promote cell adhesion.
- **Heat-activated crosslinking** facilitates cell embedding.

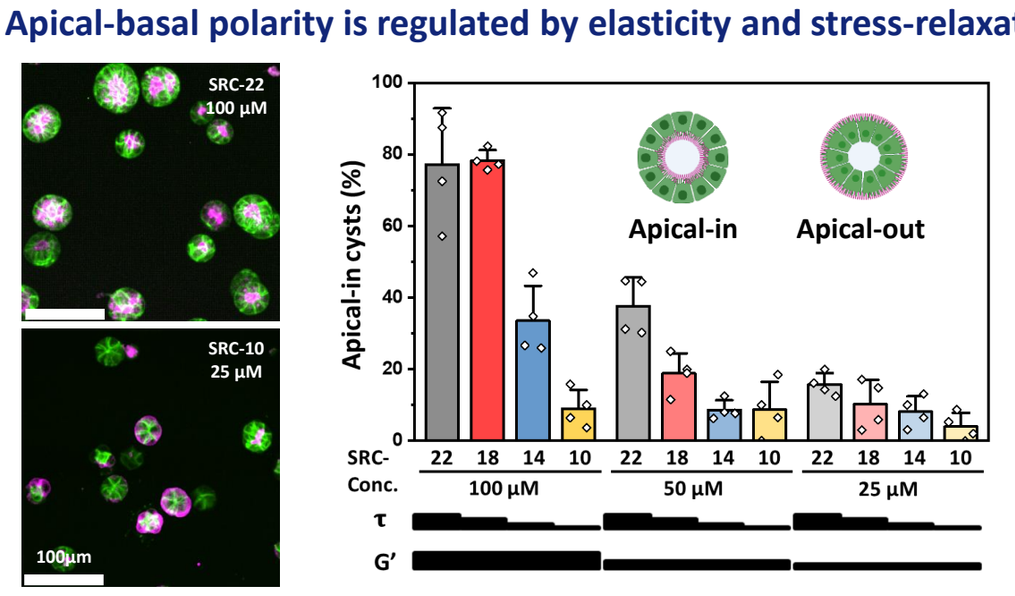


Sequence-defined mechanical properties of DyNAtrix

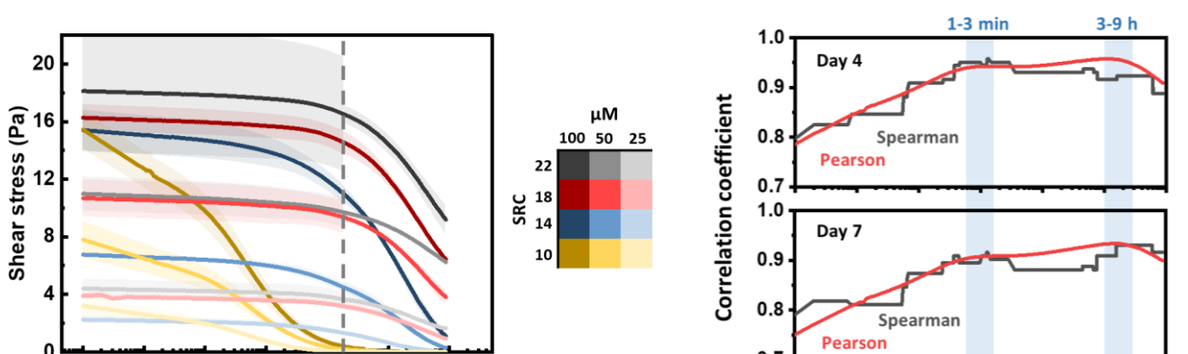


The mechanical properties of **DyNAtrix** can be tuned by varying the DNA crosslinker design and crosslinker concentration. Its stress-relaxation behavior can be modulated across **four orders of magnitude** by changing the length of the **overlap domain** within the DNA crosslinkers. In addition, the stiffness of DyNAtrix can be precisely controlled in the **ultrasoft regime**.

Apical-basal polarity is regulated by elasticity and stress-relaxation



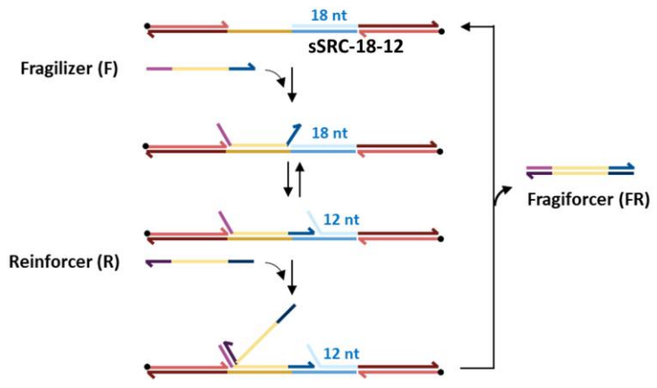
Correlation of the fraction of apical-in cysts with time-dependent shear stress reveals two mechanosensing timescales in cell polarization



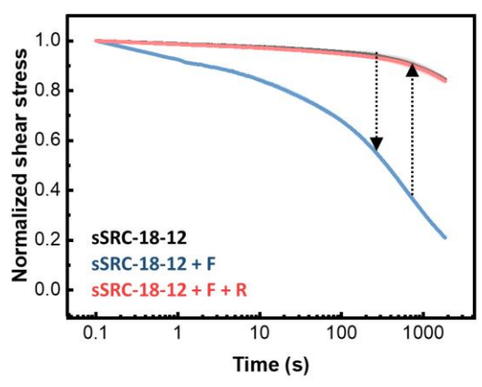
Left: Stress-relaxation curves of the 12 DyNAtrix variants.
Right: Correlation of the fraction of apical-in cysts on days 4 and 7 with the time-dependent shear stress obtained from the step-strain experiments.

In situ stress-relaxation switching triggers polarity change

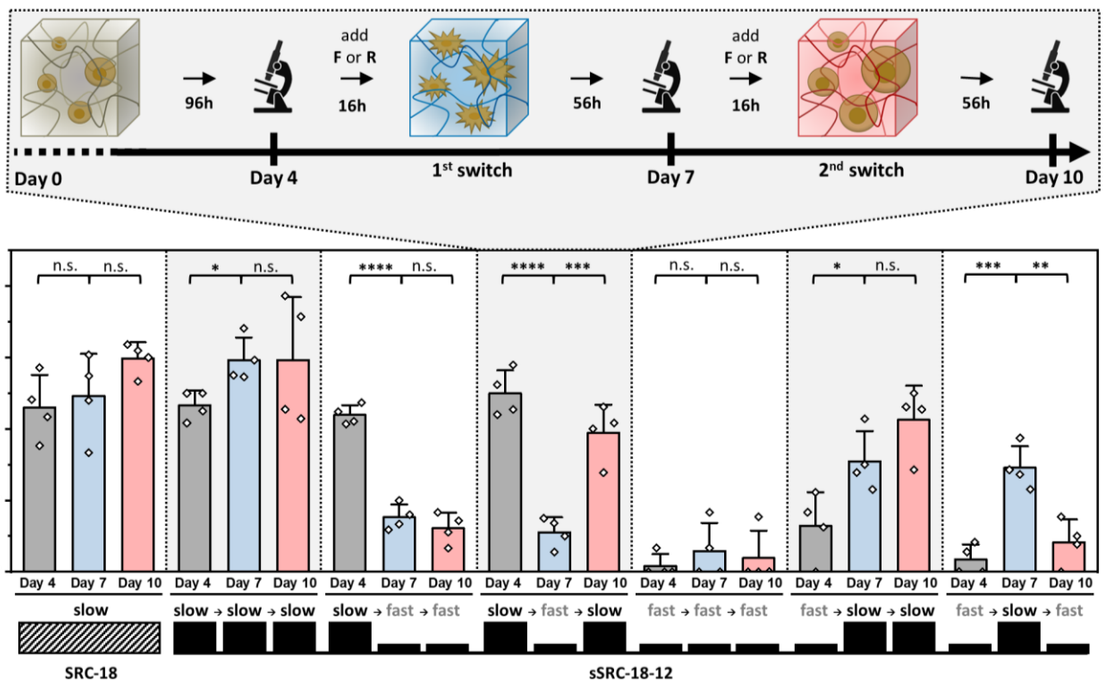
Switchable Stress-relaxation crossinker



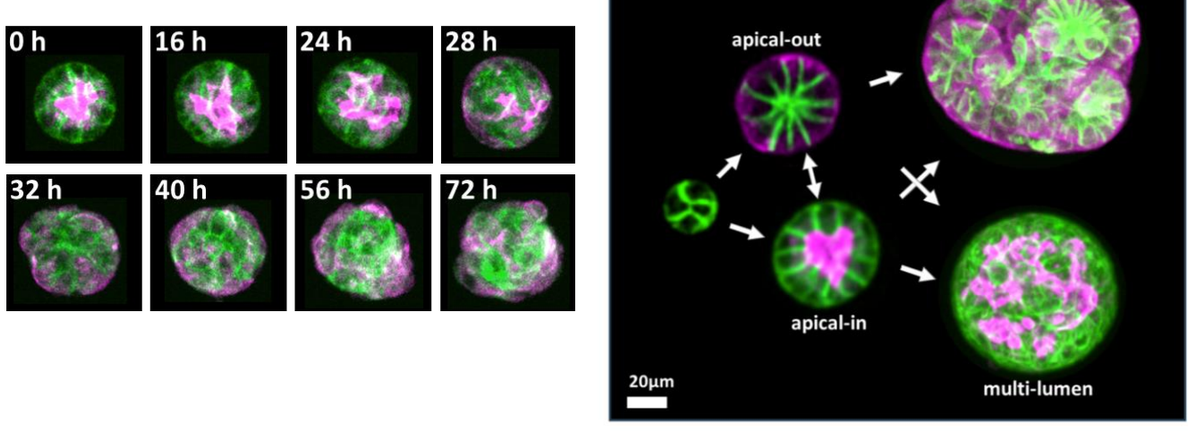
Stress-relaxation switching



In situ stress-relaxation switching during ongoing cell culture



Stress-relaxation switching induces apicobasal polarity switching



Conclusions

- **DyNAtrix provides precise dynamic control over the microenvironment around cells, enabling advanced studies in cell biology, regenerative medicine, and disease modeling.**
- **Viscoelasticity tuning exposes critical time scales of mechano-signaling.**
- **DyNAtrix enables *in-situ* stress-relaxation tuning and triggers polarity switching.**

For more information…

Our website

This study

References

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