How to create a preferred collagen organization

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Introduction
- In vitro engineered fibrous tissues lack native-like matrix anisotropy, essential for in vivo functionality and durability.
- Experiments suggest actin-mediated cell traction and associated cellular orientation affect this anisotropy.
- Hence, the ability to manipulate stress-fiber orientation may be key to develop this preferred matrix anisotropy.

Research question
- Can we guide stress-fiber orientation via cyclic straining in 3D?, and expose the underlying mechanism?

Model system
- A small-scale tissue model system was developed to enable full 3D visualization of the specimen (Fig. 1).

Analysis
- Confocal microscopy was used to visualize cell nuclei & stress-fibers; a measure for cell traction).
- Preferential stress-fiber orientation ($\alpha \pm \text{std}$) was quantified using fiber tracking software and bimodal fitting.

Results & Discussion
- Transient contraction followed by uniaxial cyclic strain induced a biaxial stress-fiber orientation, preferentially towards the constraint direction (Fig. 3, core).

Conclusion
- In 3D, cells orient perpendicular to imposed cyclic strain (strain avoidance), however, collagen contact guidance can dominate over strain avoidance.
- Results indicate the significance of scaffold directionality for obtaining a preferred matrix anisotropy in tissue-engineering applications.