Spontaneous morphogenesis of soft-fibrous tissue: cell-driven mechanical remodeling of the extra-cellular matrix

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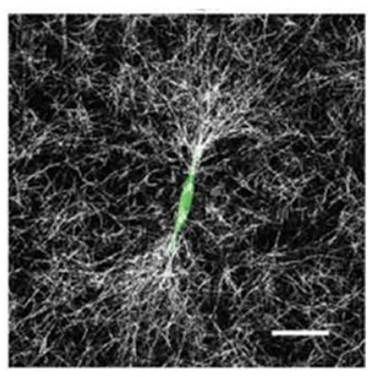
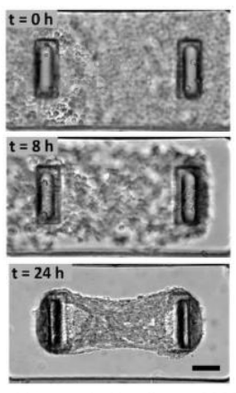
Introduction

Cell-scale ECM remodeling



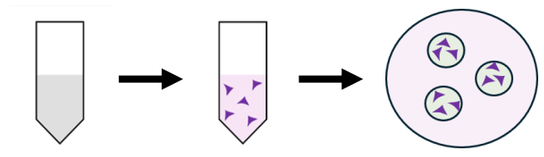
Yang et al., PNAS, 2023

Tissue-scale ECM remodeling



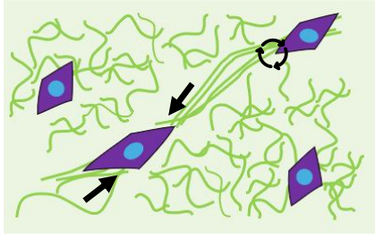
Méry et al., Nat.Com., 2022

Collagen type I acidic solution → Neutralize to pH=7 & add cells → 24 - 72 hours Incubation at 37 ºC



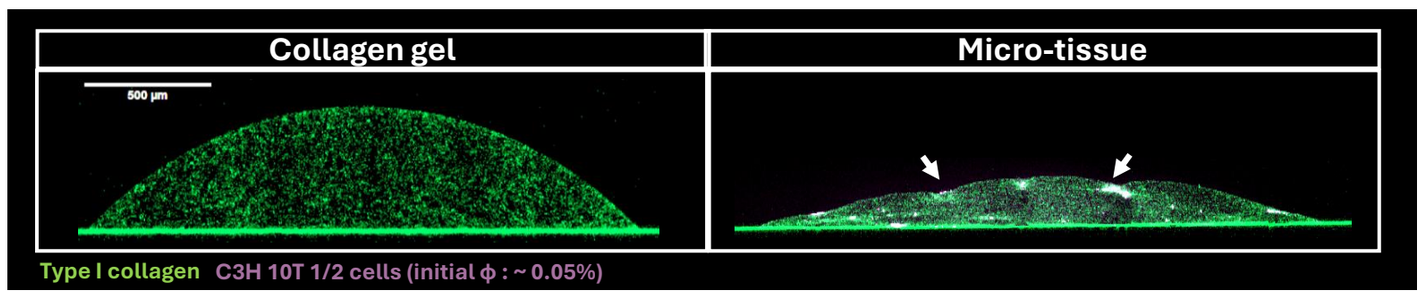
Micro-tissue side view

MSCs apply & respond to mechanical forces

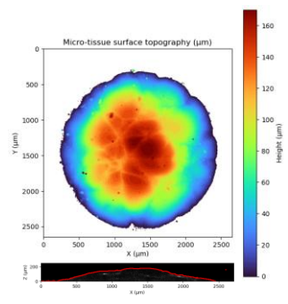


Mesenchymal stem cells (MSC)
ECM

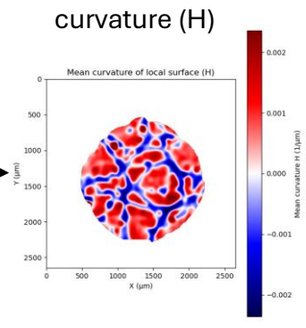
Out of plane local tissue deformations – invaginations



Surface topography

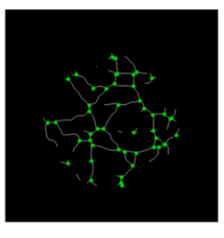


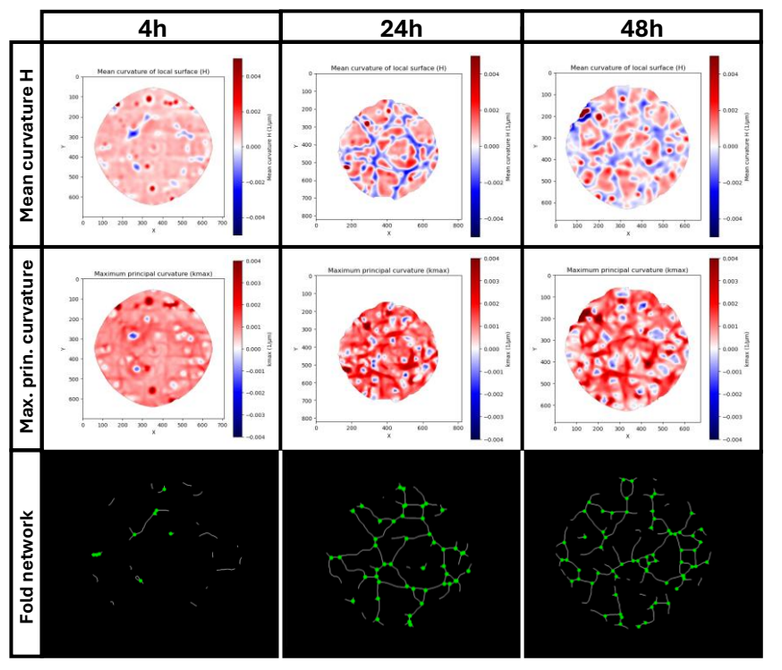
Local mean curvature (H)



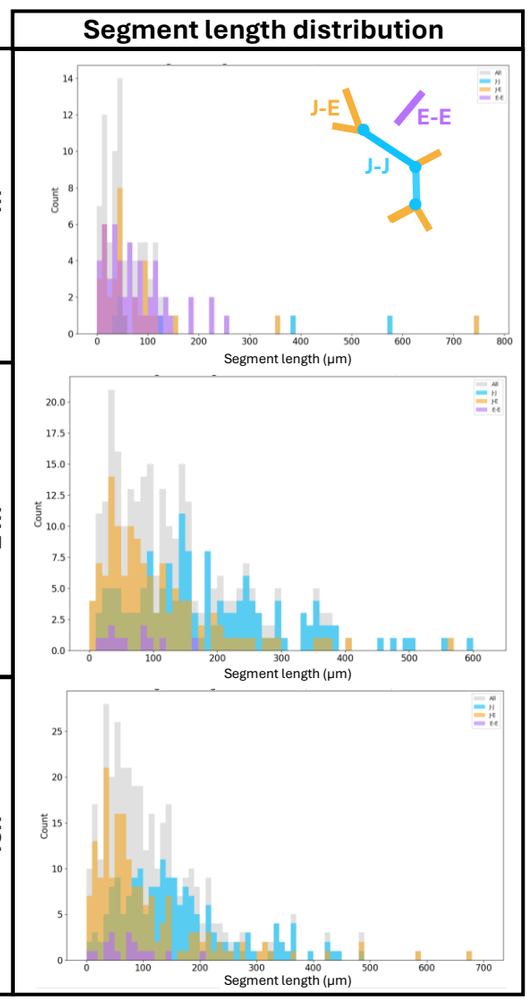
Binary mask (H<0)

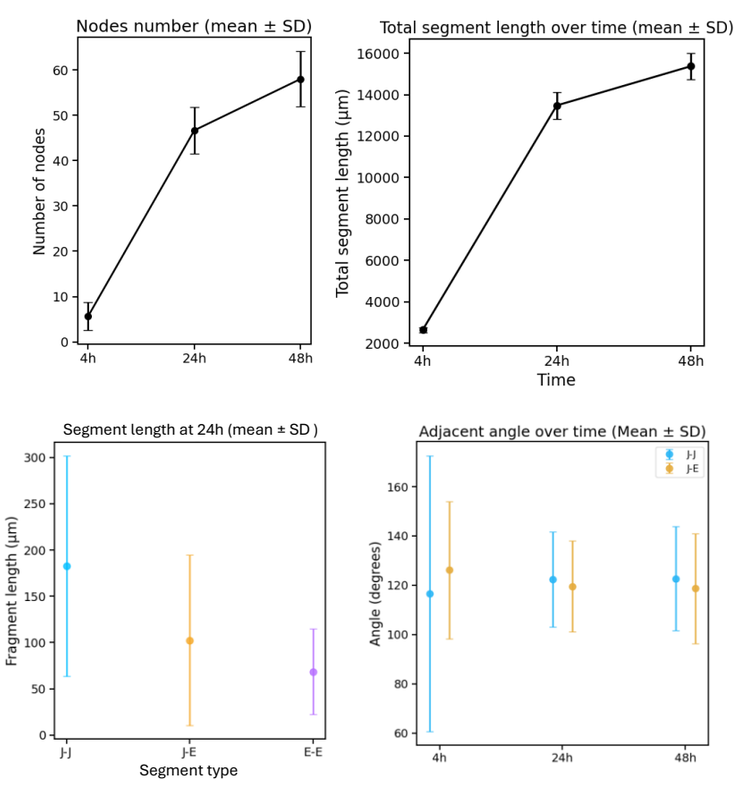
Skeletonization & network analysis





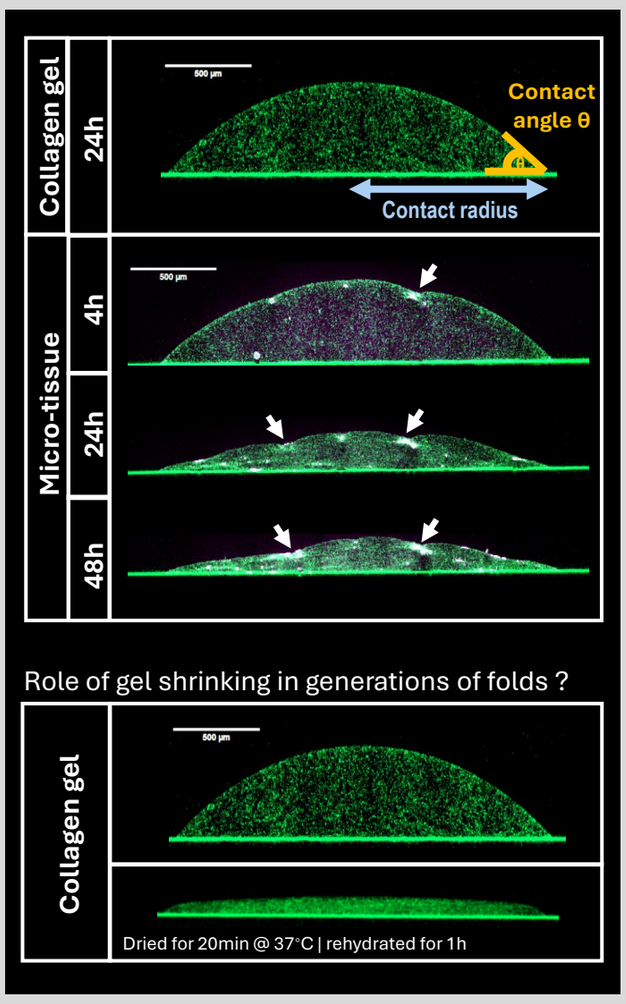
Fold network analysis



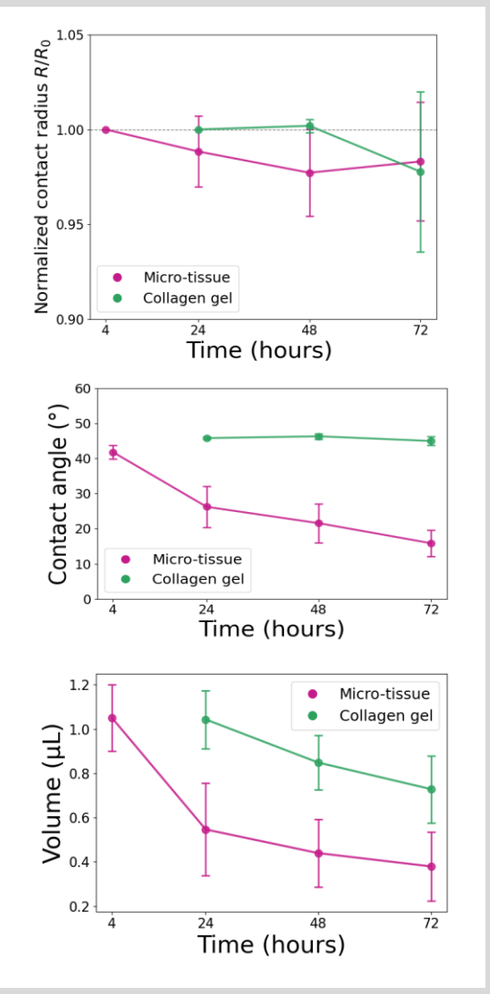


- Segment length > cell length (~50 µm)
- **Long-range communication between cells via ECM ?**
- Fold network branching at ~120°
- **Mechanical tension governs network organization ?**

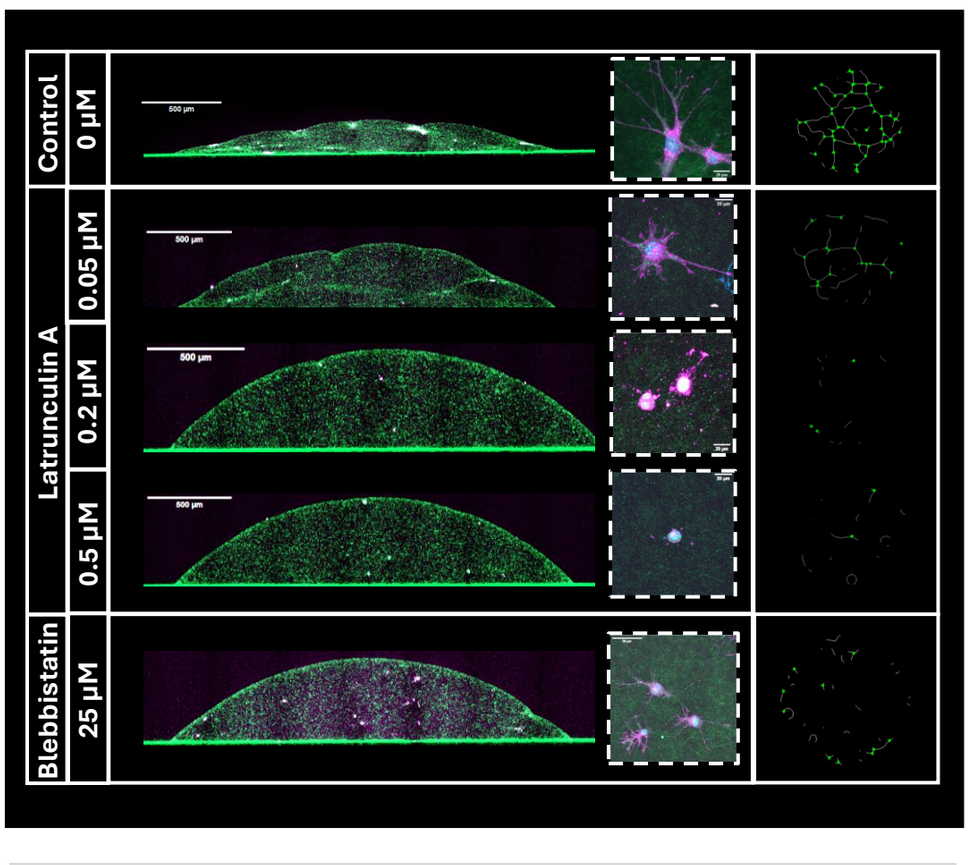
Global micro-tissue remodeling

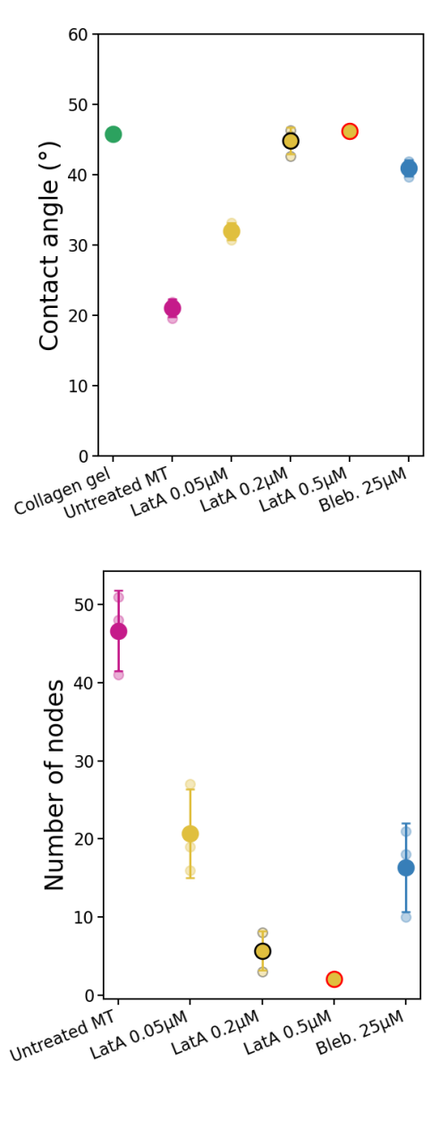


Role of gel shrinking in generations of folds ?



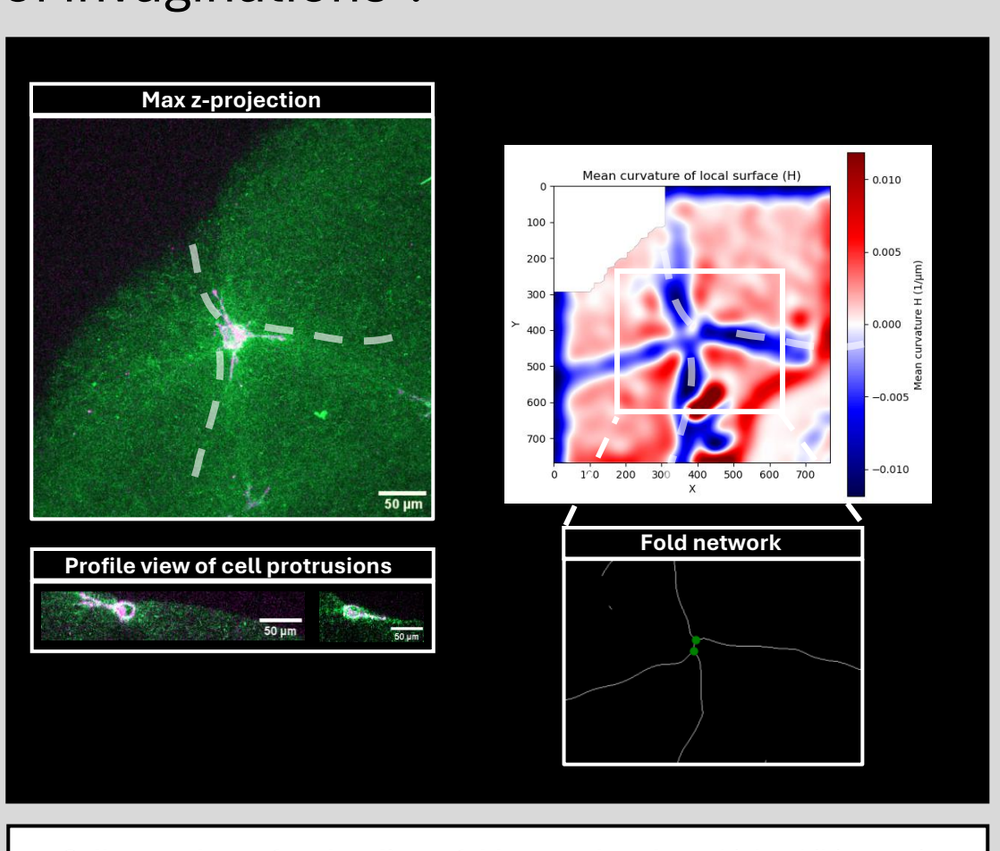
Role of actin-polymerization & myosin II activity





- Global flattening / lose of volume & fold network formation is **actomyosin dependent**
- ~5-fold increase in Young's modulus in the presence of cells → mechanical compaction of the matrix by cells ?
- Global micro-tissue flattening alone does not generate surface invaginations

What drives the formation and evolution of invaginations ?



- **Cells near the surface localize at fold-network nodes**, which exhibit negative maximal principal curvature indicating the formation of pit-like invaginations
- **Cell protrusions co-localize with fold segments**, suggesting that cells actively form/shape the fold network
- Fold segments connect cells over distances exceeding individual cell length, creating a **network that may promote long-range mechanical interactions between cell via ECM**