Modelling of Focal Adhesions Considerably Affects the Predicted Intracellular Strain Field

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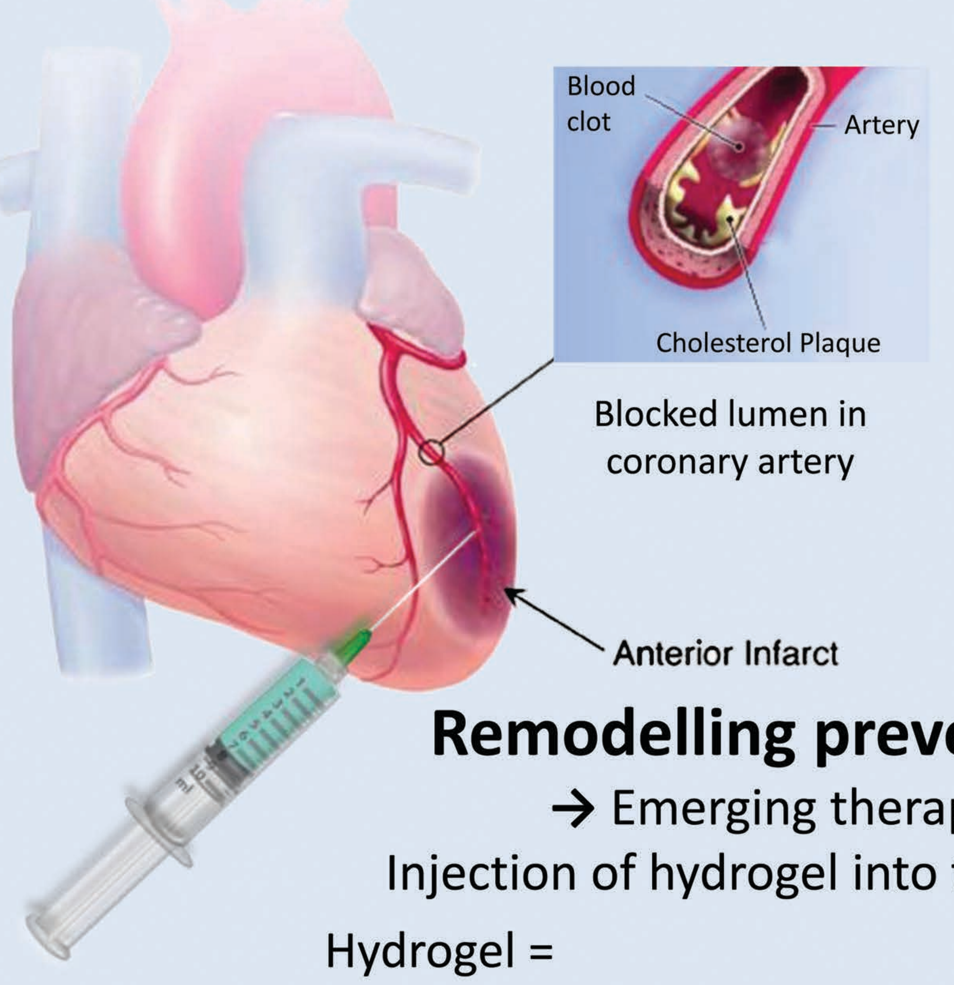
1. Context

Myocardial Infarction (heart attack)

→ **Death** of a part of the myocardium



1. Loss of contractile properties
2. Tissue stiffness and thickness modification
3. Remodelling

High risk of **heart failure**!

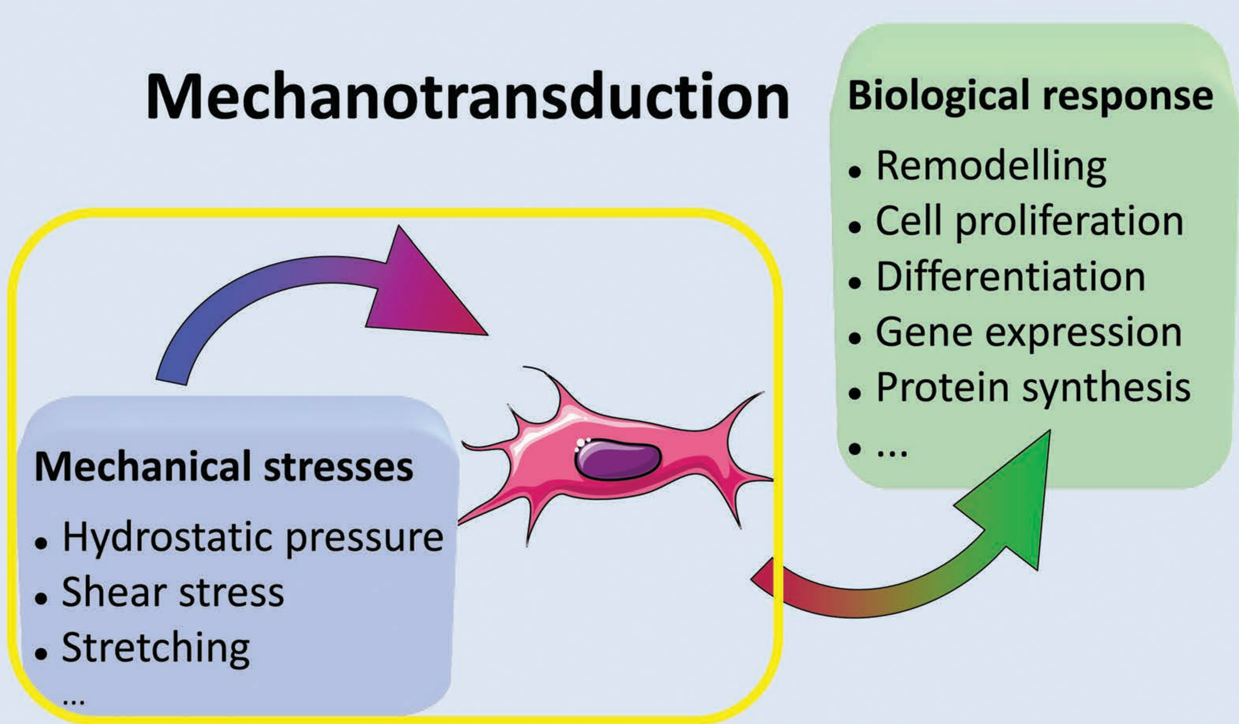
Remodelling prevention

→ Emerging therapy:
Injection of hydrogel into the infarct

Hydrogel =
- 99 % water
- Polymer

Stem cells

Mechanotransduction

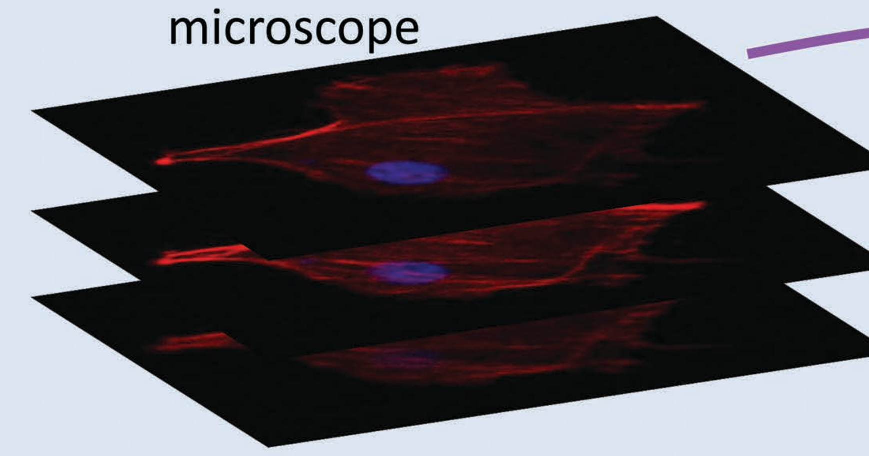


Questions

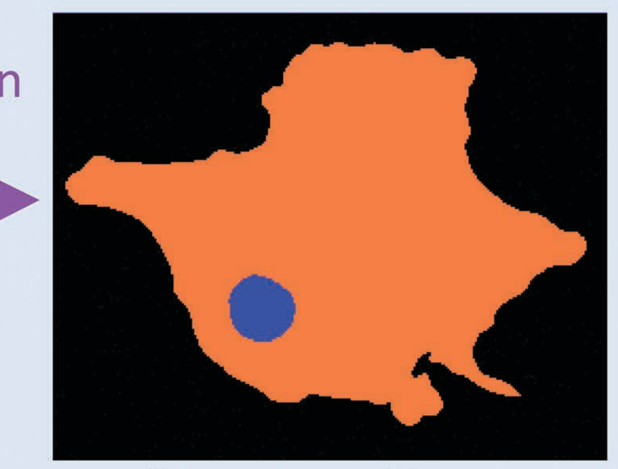
What is the effect of:
→ the **focal adhesion** (FA) modelling
→ the **structural stiffness** of the extracellular matrix (ECM) on the strain field?

2. Methods

Geometry

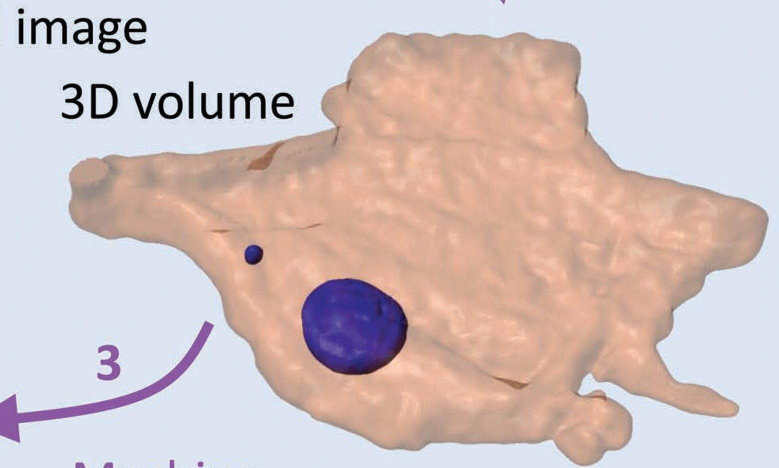


Segmentation + smoothing
1

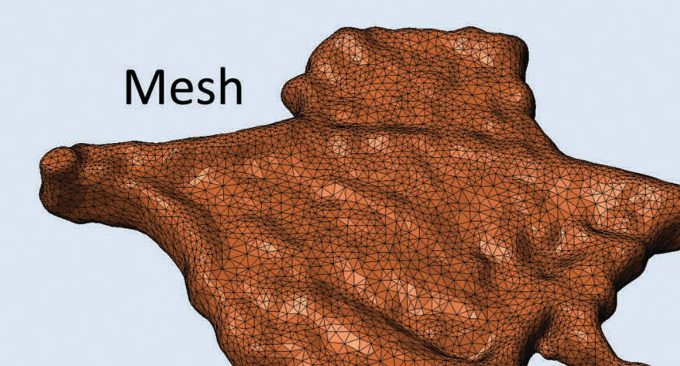


Segmented image

3D generation
2



3
Meshing



Mechanical properties

Component	Constitutive law	Parameters
Cytosol [1]	Neo-Hookean	c_{10} = 0.5 kPa κ = 9.7 kPa
Nucleus [4]	Neo-Hookean	c_{10} = 0.8 kPa κ = 16.4 kPa
Membrane	Hooke (linear)	E = 0.1-100 kPa ν = 0.47

Three models of cell-substrate contact

Uneven with focal adhesions (**UFA**)
→ Bottom of the cell is uneven (following the microscope image).
→ FA are located at the contact areas with the ECM.

Even with focal adhesions (**EFA**)
→ Bottom of the cell is even (smoothed).
→ FA are located at the same location as UFA.

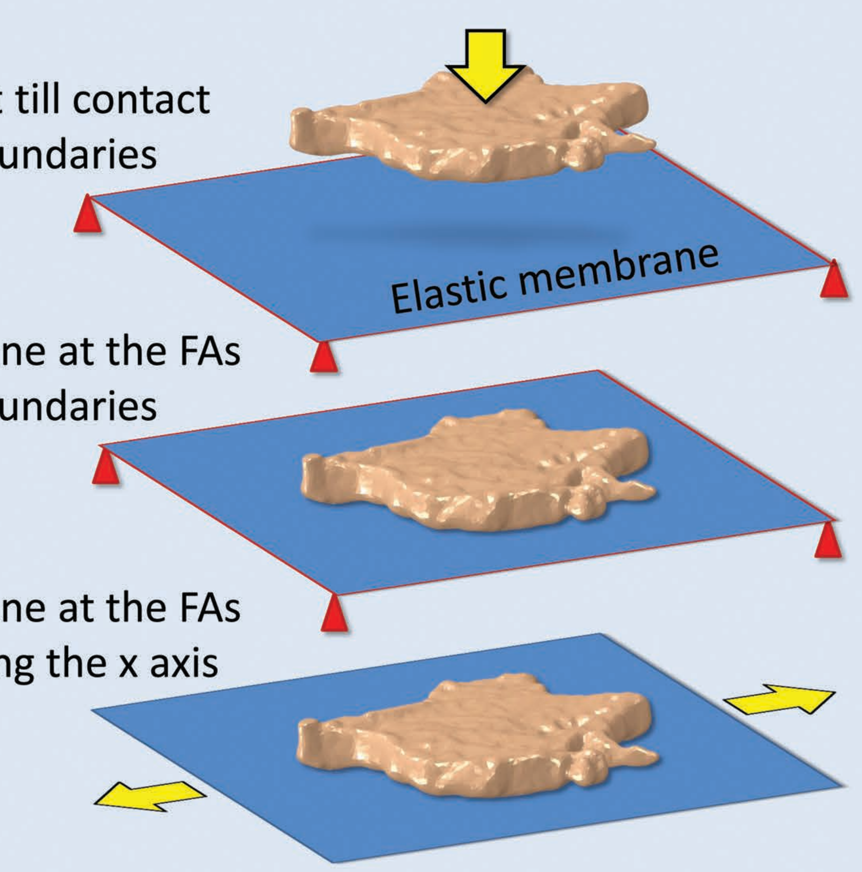
Even with large contact (**ELC**)
→ Bottom of the cell is even (smoothed).
→ Large contact area between the bottom and the ECM.

Boundary conditions

Step 1: **Contact initiation**
- Cell: vertical displacement till contact
- Membrane: fixed at its boundaries

Step 2: **Tie constraint**
- Cell: glued to the membrane at the FAs
- Membrane: fixed at its boundaries

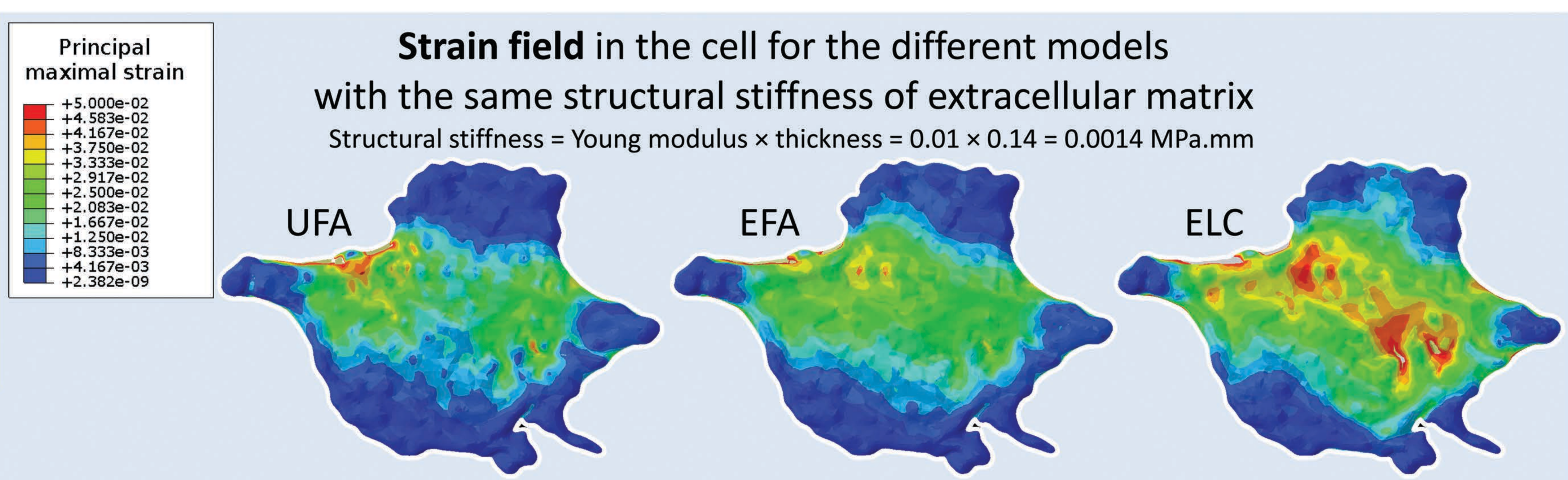
Step 3: **Stretching**
- Cell: glued to the membrane at the FAs
- Membrane: stretched along the x axis



3. Results

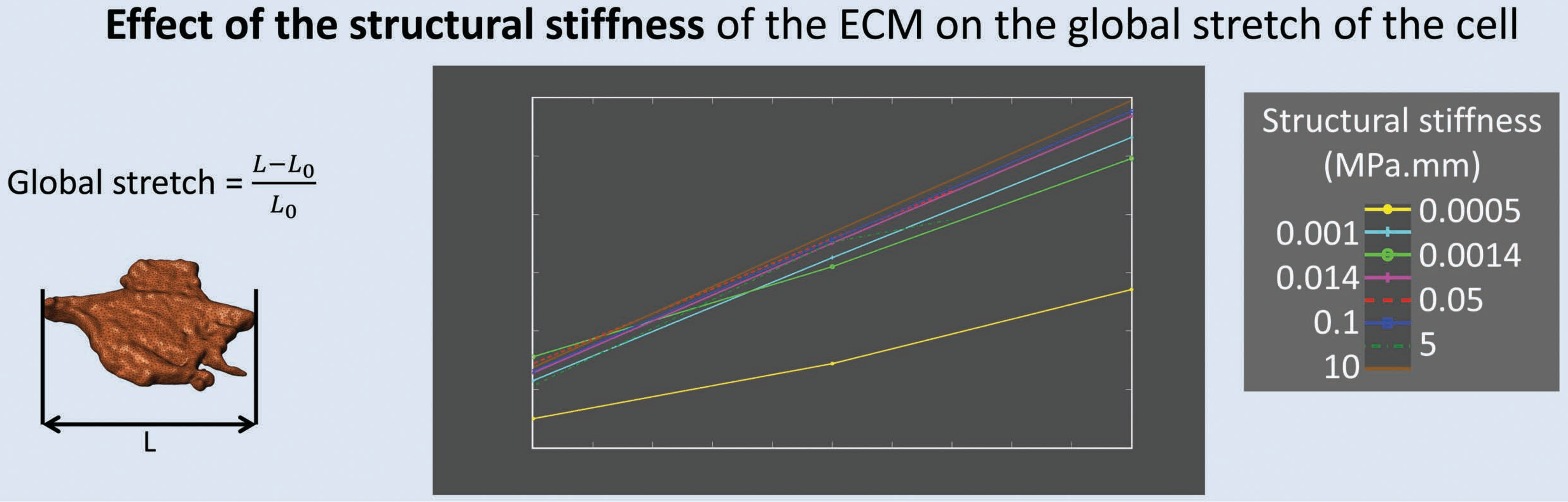
Strain field in the cell for the different models
with the same structural stiffness of extracellular matrix

Structural stiffness = Young modulus × thickness = 0.01 × 0.14 = 0.0014 MPa.mm



Effect of the structural stiffness of the ECM on the global stretch of the cell

Global stretch = $\frac{L-L_0}{L_0}$



4. Conclusion

✓ **Global strain** of the cell depends of structural properties of the extra-cellular matrix.
→ The stiffness of the ECM affects the mechanical response of the cell.

✓ **Strain field** in the cell depends on the FA position/surface and is non-homogeneous.
→ Location of FAs have a significant effect on the strain field.

References

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