Approximations of cell-induced phase transitions in fibrous biomaterials: Γ-convergence analysis

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Introduction

Through mechanical forces, biological cells remodel the surrounding collagen matrix, generating localized deformations, which are regions with high densification and fiber alignment.

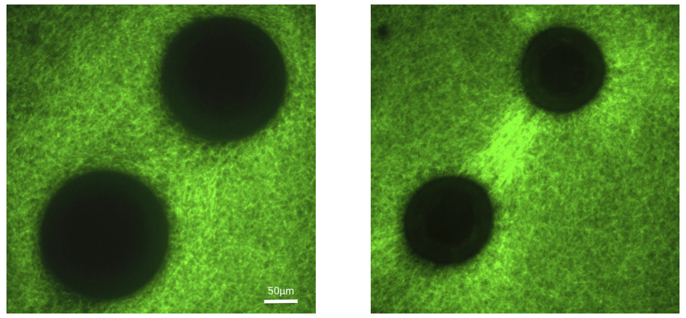

Figure 1: Using experiments with active particles in [1], we have shown that localized deformations can be formed by mechanical forces. Left uncontracted active particles, Right contracted. Density in the bright region is from 3 to 6 times higher than outside.

In [1] the mechanical behaviour of the extracellular matrix (ECM) is modelled and analysed from a macroscopic perspective, using the theory of nonlinear elasticity for phase transitions. The mathematical model used is a variational problem involving a non convex multi-well strain-energy function, regularized by a higher order term:

$$\Psi[\boldsymbol{u}] = \int_\Omega W(\nabla \boldsymbol{u}(\boldsymbol{x})) + \Phi(\nabla \boldsymbol{u}(\boldsymbol{x})) + \frac{\varepsilon^2}{2}|\nabla\nabla \boldsymbol{u}(\boldsymbol{x})|^2 d\boldsymbol{x}, \tag{1}$$

with $\boldsymbol{u} \in H^2(\Omega)^2$ and $\boldsymbol{u}$ satisfies some appropriate boundary conditions, $W + \Phi$ is the strain energy function, Φ is a function that penalizes the interpenetration of matter and is allowed to grow faster than W as the volume ratio approaches zero, and $\varepsilon > 0$ is a fixed real parameter (related to characteristic fiber length).

Our objective: We seek solutions of the minimizing problem

$$\min_{\boldsymbol{u}\in\mathbb{A}(\Omega)} \Psi[\boldsymbol{u}], \quad \mathbb{A}(\Omega) \subset H^2(\Omega)^2 \tag{2}$$

To approximate minimizers of the continuous problem a FE method with **lower regularity** is employed:

$$\min_{\boldsymbol{u}_h\in\mathbb{A}_h(\Omega)} \Psi_h[\boldsymbol{u}_h], \quad \mathbb{A}_h(\Omega) \subset H^1(\Omega)^2 \tag{3}$$

$\mathbb{A}_h(\Omega)$ is the discrete function space, Ψ has been modified appropriately. We would like to justify mathematically the above procedure, by showing that appropriate numerical approximations indeed converge in the limit to minimisers of the continuous problem, [2].

Discretization of the Energy Functional

- Why a nonconforming method? For computational efficiency and implementation simplicity.
- The energy functional Ψ should be modified to account for possible discontinuities of derivatives at the element faces.
- The modification of total potential energy will affect only the higher gradient term (Similar to the C^0 Discontinuous Galerkin method for the linear biharmonic problem):

$$\Psi_h^{ho}[\boldsymbol{u}_h] = \frac{1}{2}\sum_{K\in T_h}\int_K |\nabla\nabla \boldsymbol{u}_h|^2 d\boldsymbol{x} - \sum_{e\in E_h^i}\int_e \{\!\{\nabla\nabla \boldsymbol{u}_h\}\!\} \cdot [\![\nabla \boldsymbol{u}_h \otimes \boldsymbol{n}_e]\!] ds + \sum_{e\in E_h^i}\frac{\alpha}{h_e}\int_e |[\![\nabla \boldsymbol{u}_h]\!]|^2 ds,$$

Where $\{\!\{\cdot\}\!\}$ and $[\![\cdot]\!]$ are the average and jump operators respectively, α is a stabilization parameter and h_e is a measure of the cell size.

Convergence of discrete minimizers

For the convergence we need to prove **Γ-convergence** and **Discrete Compactness**. For this purpose the higher order terms, see Ψ_h^{ho}, are represented using the discrete second gradient and appropriate lifting operators as:

$$\Psi_h^{ho}[\boldsymbol{u}_h] = \frac{1}{2}\int_\Omega |\boldsymbol{G}_h(\nabla \boldsymbol{u}_h)|^2 - |\boldsymbol{R}_h(\nabla \boldsymbol{u}_h)|^2 d\boldsymbol{x} + \sum_{e\in E_h^i}\frac{\alpha}{h_e}\int_e |[\![\nabla \boldsymbol{u}_h]\!]|^2, \tag{4}$$

Then one can show

$$\boldsymbol{G}_h(\nabla \boldsymbol{u}_h) \rightharpoonup \nabla\nabla \boldsymbol{u}, \text{ as } h \to 0 \tag{5}$$

Assume Φ has polynomial growth: From Poincaré-type inequalities for broken Sobolev Spaces the convergence of the lower order terms is deduced

$$\int_\Omega W(\nabla \boldsymbol{u}_h) + \Phi(\nabla \boldsymbol{u}_h) \to \int_\Omega W(\nabla \boldsymbol{u}) + \Phi(\nabla \boldsymbol{u}), \quad \text{when } \boldsymbol{u}_h \to \boldsymbol{u} \text{ in } H^1(\Omega)^2, \tag{6}$$

as $h \to 0$, (Vitali's convergence Theorem). For the lim inf inequality the latter two equations are used. From a diagonal argument the lim sup inequality holds which implies

$$\Psi_h \xrightarrow{\Gamma} \Psi. \tag{7}$$

Large deformations require suitable penalty functions to avoid interpenetration of matter. Adding a polyconvex function Φ with exponential growth, i.e.

$$\Phi(J) = e^{a(J+b)}, \quad J = \det(\mathbf{1} + \nabla \boldsymbol{u}), \quad a, b \in \mathbb{R}, \tag{8}$$

extra embedding results are needed to show that Ψ_h Γ−converges to Ψ. For this purpose, we have proved an adaptation of Trudinger's embedding theorem for Orlicz spaces to the piecewise polynomial spaces admitting discontinuities in the gradients.

From the new embedding uniform-integrability for Φ is recovered and can be proved that

$$\Phi(\nabla \boldsymbol{u}_h) \to \Phi(\nabla \boldsymbol{u}), \quad \boldsymbol{u}_h \to \boldsymbol{u} \text{ in } H^1(\Omega)^2 \tag{9}$$

Bounds for the total variation for the gradient of the discrete functions play a key role in the desired compactness.

Main result

Theorem 1. Let $(\boldsymbol{u}_h) \subset \mathbb{A}_h(\Omega)$ be a sequence of absolute minimizers of Ψ_h, namely

$$\Psi_h[\boldsymbol{u}_h] = \inf_{\boldsymbol{w}_h\in\mathbb{A}_h(\Omega)} \Psi_h[\boldsymbol{w}_h] \le C,$$

C independent of h. Then, there exists $\boldsymbol{u} \in \mathbb{A}(\Omega)$ such that

$$\boldsymbol{u}_h \to \boldsymbol{u}, \quad \text{in } H^1(\Omega)^2, \quad \text{and} \quad \Psi[\boldsymbol{u}] = \min_{\boldsymbol{w}\in\mathbb{A}(\Omega)} \Psi[\boldsymbol{w}].$$

Computational Experiments

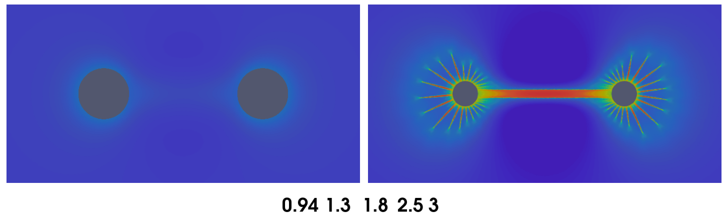

Figure 2: Each circular cavity contracts homogeneously and deforms the matrix, plot in the deformed state. The initial radius is r_c, the deformed $0.8r_c$ (left) and $0.4r_c$ (right). Centers are located at $(-2.5r_c, 0)$; $(2.5r_c, 0)$. Scalebar: ratio of deformed to undeformed density, $\varepsilon = 0.005r_c$.

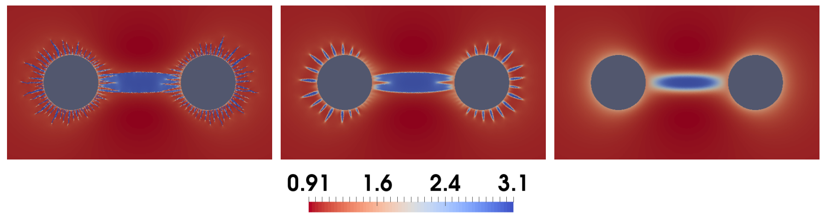

Figure 3: The parameter ε can be considered as an internal length scale: Left: $\varepsilon = 0$, middle: $\varepsilon = 0.005r_c$ and right $\varepsilon = 0.05r_c$, plots are in the reference configuration under 50% contraction, deformed radius $= 0.5r_c$. Scalebar: ratio of deformed to undeformed density.

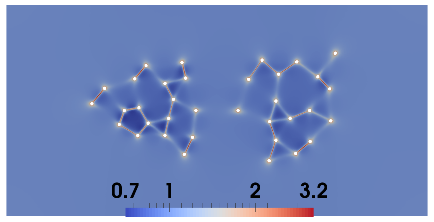

Figure 4: Simulating matrix density in the deformed state under multiple cells contraction.

References

[1] G. Grekas, M. Proestaki, P. Rosakis, J. Notbohm, C. Makridakis, and G. Ravichandran. Cells exploit a phase transition to establish interconnections in fibrous extracellular matrices. *arXiv preprint arXiv:1905.11246*, 2019.

[2] G. Grekas, K. Koumatos, C. Makridakis, and P. Rosakis. Approximations of cell-induced phase transitions in fibrous biomaterials: Gamma-convergence analysis. *arXiv preprint arXiv:1907.01382*, 2019.