Total: 8.5

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COMPUTATIONAL MECHANICS

Traction Force Microscopy

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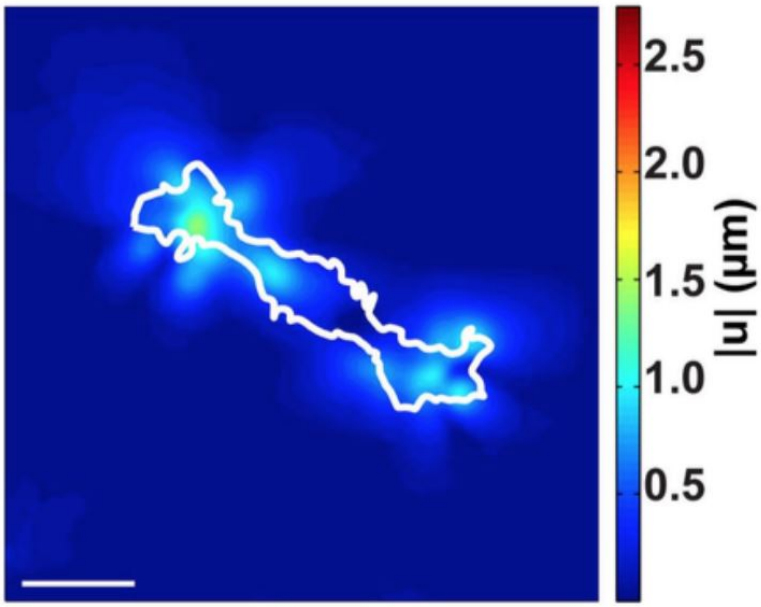
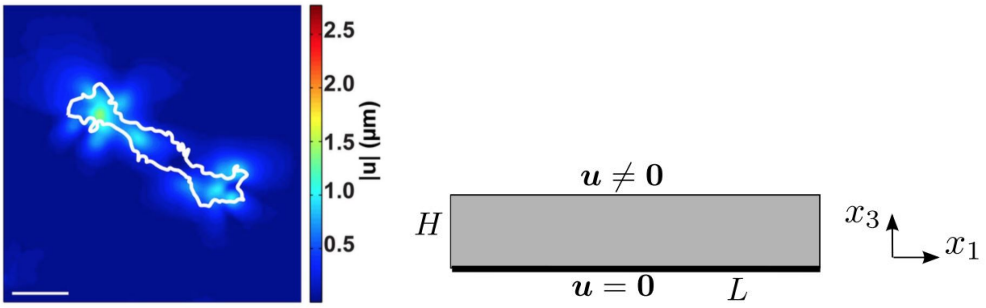


Academic year 2018-2019

ABSTRACT: In this coursework from the subject Computation Mechanics we are going to analyse the article by Toyjanova et al. about Traction Force Microscopy (TFM).

Traction Force Miscroscopy consists on measuring the tractions $\boldsymbol{t}$ that cells exert on an elastic substrate from the measurements of the displacements that they create on the top of this substrate. The article by Toyjanova et al. proposes a methodology to compute these tractions.



(a) Map of the displacements. (b) Cross-section of the gel substrate.

FIG. 1: Map of displacements and cross section of the PA gel substrate.

1. **Explain the methodology described in the article for computing the stress field $\boldsymbol{\sigma}$.**

   The problem consists on computing the forces that a cell exerts when it is placed in a material. To study this, a cell is put on a Polyacrilamide (PA) gel, like the cross section we can see in Figure 1. Characterising these tractions or forces exerted by a cell onto the PA gel, we can study its mechanical behaviour, which is interesting for applications such as biomedicine.

   The first thing that we need to compute the stress field $\boldsymbol{\sigma}$ is the deformation field that the cell produces over the PA gel. This can be obtained with a new Digital Volume Correlation method called First Iterative Digital Volume Correlation (FIDVC), that allows us to obtain a more accurate deformation field $\boldsymbol{u}$.

   After obtaining $\boldsymbol{u}$, the deformation gradient tensor in the substrate is simply computed as

   $$\boldsymbol{F} = \boldsymbol{I} + \nabla \boldsymbol{u},$$

   where $\nabla \boldsymbol{u}$ is the deformation gradient. The Lagrangian strain tensor is also computed as:

   $$\boldsymbol{E} = \frac{1}{2}(\boldsymbol{F}^T \cdot \boldsymbol{F} - \boldsymbol{I}) = \frac{1}{2}(\nabla \boldsymbol{u} + (\nabla \boldsymbol{u})^T + \nabla \boldsymbol{u} \cdot (\nabla \boldsymbol{u})^T).$$

   Now that we have obtained the Lagrangian strain tensor $\boldsymbol{E}$, we will proceed to compute the stress tensor $\boldsymbol{\sigma}$. Because of the properties of the PA gel that we are working with, the best possible choice to relate the stress and the strain tensor is to use the Neo-Hookean constitutive law:

   $$\boldsymbol{\sigma} = \frac{\mu}{J^{5/3}} \left(\boldsymbol{B} - \frac{1}{3} \operatorname{Tr}(\boldsymbol{B}) \cdot \boldsymbol{I} \right) + K(J-1)\boldsymbol{I},$$

   where J is the Jacobian determinant of the deformation gradient tensor $\boldsymbol{F}$, $\boldsymbol{B}$ is the left Cauchy Green's tensor and μ and K are the material's shear and bulk modulus, respectively.

2. **In the paragraph "Global Force and Moment Balance", the authors claim that the resulting tractions are equilibrated. What do they mean by this? Do you think that these tractions will be equilibrated for general displacements?**

   They see that the sum of all tractions is zero by computing the sum of all forces and moments acting on any given control volume inside each PA gel (before and after placing the cell). In all the experiments they see that this sum is always under a very low threshold (10^{-9} N for the forces and 10^{-14} $N \cdot m$ for the moments), considering it noise. However, these tractions might not be equilibrated for general displacements. Because no balance law is imposed

3. **Do you think that the stress field retrieved by the authors is in static equilibrium, that is, it satisfies $\nabla \cdot \boldsymbol{\sigma} = \mathbf{0}$? Justify why.**

   Yes, it is in static equilibrium. We can see it from the motion equation:

   $$\nabla \cdot \boldsymbol{\sigma} + \rho \boldsymbol{b} = \rho \frac{\partial^2 \boldsymbol{u}}{\partial \boldsymbol{x}^2}$$

   Due to the small weight of the cells, the external forces $\boldsymbol{b}$ applied to them can be neglected. We can also assume that the acceleration is zero because the size that these cells have with respect to the gel is very small.

   Hence, we obtain the static equilibrium equation:

   $$\nabla \cdot \boldsymbol{\sigma} = 0$$ But this equation is never imposed....

4. **Implement a linear finite element version of the algorithm. For this,**

   (a) **Use a two-dimensional plain-strain problem with domain $(x_1, x_3) \in [0, L] \times [0, H]$, representing a (x_1, x_3) cross-sections, and with one layer of elements along x_3.**

   (b) **Prescribe the displacements of the nodes at $x_3 = 0$ with a zero value, and those at $x_3 = H$ with arbitrary values.**

   (c) **Compute the force vectors (reactions $\boldsymbol{r}_i$) that create the displacement that you have prescribed.**

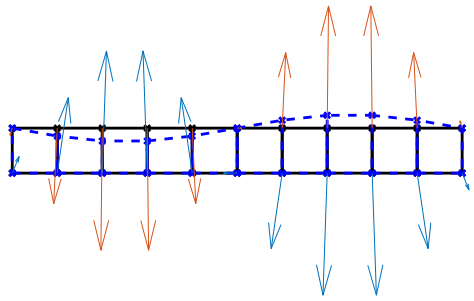
5. **Compare the forces at the top layer $x_3 = H$ using $L = 10$, $H = 1$ and the following two approaches with three different discretization $n_x = 10, 20, 50$, $n_y = 1, 2, 5$.**

   (a) **(Methodology of the paper) Computing the stresses $\boldsymbol{\sigma}$, and obtaining the traction field as $\boldsymbol{t} = \boldsymbol{\sigma n}$. Convert these tractions to nodal contributions, $\boldsymbol{r_i} = \int_{\partial\Omega(x_3=H)} N_i \boldsymbol{t} \, d\Gamma$.**

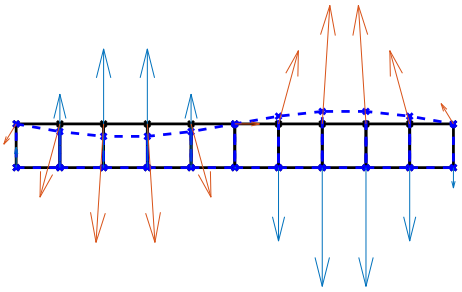
   (b) **Compute the nodal reactions $\boldsymbol{r}_i$ at the top layer using the implemented FEM.**

On the one hand, as the FEM method starts from the static equilibrium equation $\nabla \cdot \boldsymbol{\sigma} = 0$, the reactions will always be compensated, no matter the displacement. On the other hand, the paper's method only considers the constitutive law disregarding the static equilibrium equation. Although the authors claim that the final stress field is in static equilibrium, that does not mean that the reactions compensate for any general displacement, because there can be internal forces that compensate this reactions. This fact can be observed in the following figure, were the dash lines show the imposed displacements and the red and blue arrows correspond to the top and bottom boundary reactions, respectively.

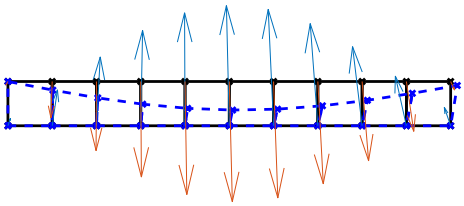
Yes



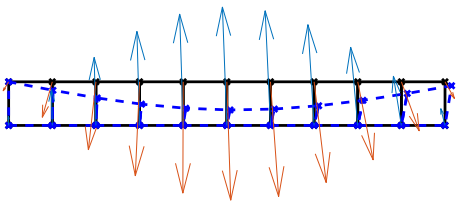
(a) FEM method with compensation of reactions using $u_x = 0$ and $u_y = -0.6 \cdot sin(2\pi x/L)$



(b) Paper's method with compensation of reactions using $u_x = 0$ and $u_y = -0.6 \cdot sin(2\pi x/L)$



(c) FEM method with compensation of reactions using $u_x = x/2$ and $u_y = -0.6 \cdot sin(\pi x/L) - 0.3x$



(d) Paper's method with no compensation of reactions using $u_x = x/2$ and $u_y = -0.6 \cdot sin(\pi x/L) - 0.3x$

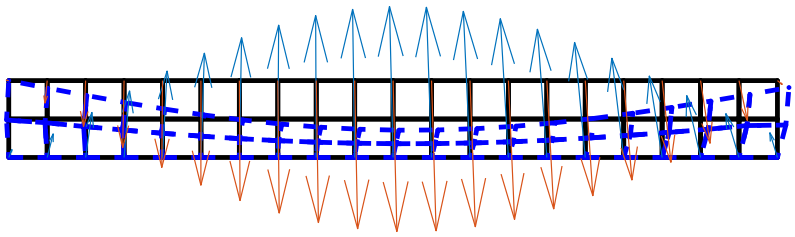
FIG. 2: Computation of the reactions along the boundary using $n_x = 10$ and $n_y = 1$

In the cases (a) and (c), since we are using the FEM method, reactions are compensate (the modulus of the sum of all reactions are below 10^{-16} in both cases).

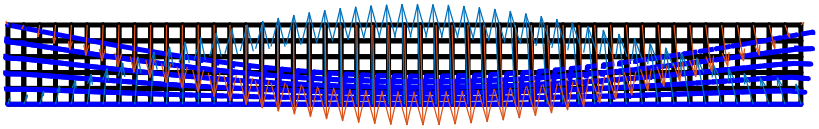
In the case (b), the modulus of the sum of all reactions is $2.6 \cdot 10^{-6}$, that can be considered negligible. However, in the case (d), it is 0.17, which means that the reaction don't compensate.

Also, in FEM nodal equilibrium is imposed, with stresses at the Gauss points. In paper's method, stresses and tractions are computed at the nodes. How have you averaged the discontinuous tractions to the nodes?

Let's recall that for $n_y > 1$, the methodology used in the paper cannot be applied because the stress field is computed using only the displacements along the boundary, disregarding the interior nodes. Nevertheless, the FEM method takes them into account and so, we can compute the reactions along the boundary for more than one layer in the y axis, as we can see below.



(a) FEM method with $n_x = 20$ and $n_y = 2$



(b) FEM method with $n_x = 50$ and $n_y = 5$

FIG. 3: Compensation of reactions using $u_x = x/2$ and $u_y = -0.6 \cdot sin(\pi x/L) - 0.3x$

6. **Comment on the accuracy limitations of the methodology followed above. Can you think on an alternative strategy in order to compute the tractions $\boldsymbol{t}$?**

Here we present different accuracy limitations for each of the methods (assuming small deformations, because the FEM method that we have doesn't work for large deformations). In both cases we will have numerical errors due to:

- The number of nodes of the mesh (the more nodes we have, the less error we will get).
- The numerical integration and the shape functions, used in the FEM method to compute K and f (in order to solve the linear system $Ku = f$) and in the paper's method to compute the reactions.

3x3 Gauss quadrature integrates exactly

In addition, the paper's method also has the approximation of the gradient of the deformations as an accuracy limitation.

Moreover, an alternative strategy to compute the tractions is using Lagrange Multipliers, as we are going to explain:

First, we will use that we are in static equilibrium:

$$\nabla \cdot \boldsymbol{\sigma} = 0$$

If we now multiply by test functions of H_0^1 and integrate over the domain, we obtain:

$$\int_\Omega \boldsymbol{v} \cdot (\nabla \cdot \boldsymbol{\sigma}) \, d\Omega = 0$$

Applying then the identity: $\nabla \cdot (\boldsymbol{v} \otimes \boldsymbol{\sigma}) = \boldsymbol{v} \cdot (\nabla \cdot \boldsymbol{\sigma}) + \nabla \boldsymbol{v} : \boldsymbol{\sigma}$, we obtain:

Should be dot product

$$\int_\Omega \nabla \cdot (\boldsymbol{v} \otimes \boldsymbol{\sigma})\ d\Omega - \int_\Omega \nabla \boldsymbol{v} : \boldsymbol{\sigma}(\boldsymbol{u})\ d\Omega = 0$$

We now apply the Divergence Theorem, the boundary conditions ($\boldsymbol{\sigma} \cdot \boldsymbol{n} = \boldsymbol{t}_N$) and the fact that $v \in H_0^1$:

$$\int_\Omega \nabla \boldsymbol{v} : \boldsymbol{\sigma}(\boldsymbol{u})\ d\Omega - \int_{\Gamma_N} \boldsymbol{v} \cdot \boldsymbol{t}_N\ dS = 0$$

Now, if we split the matrix $\nabla \boldsymbol{v}$ into a symmetric part $\varepsilon(\boldsymbol{v})$ and a skew-symmetric part $\boldsymbol{A}(\boldsymbol{v})$, i.e. $\nabla \boldsymbol{v} = \varepsilon(\boldsymbol{v}) + \boldsymbol{A}(\boldsymbol{v})$, we have that, by the definition of ":", $\boldsymbol{A}(\boldsymbol{v}) : \boldsymbol{\sigma}(\boldsymbol{u}) = 0$.

Therefore, we have obtained the weak form: Find $\boldsymbol{u} \in H^1(\Omega)$ s.t. $\boldsymbol{u} = \boldsymbol{u}_D$ on Γ_D and

$$\int_\Omega \varepsilon(\boldsymbol{v}) : \boldsymbol{\sigma}(\boldsymbol{u})\ d\Omega - \int_{\Gamma_N} \boldsymbol{v} \cdot \boldsymbol{t}_N\ dS = 0$$

for every $\boldsymbol{v} \in H_0^1(\Omega)$ with $\boldsymbol{v} = 0$ in Γ_D.

Here, we can define $\boldsymbol{\lambda} = -\boldsymbol{t}_N$ as the Lagrange multipliers. Hence, we have the equation:

$$\int_\Omega \varepsilon(\boldsymbol{v}) : \boldsymbol{\sigma}(\boldsymbol{u})\ d\Omega + \int_{\Gamma_N} \boldsymbol{v} \cdot \boldsymbol{\lambda}\ dS = 0$$

Now, we don't have enough equations to solve for the two unknowns $\boldsymbol{u}$ and $\boldsymbol{\lambda}$. So, to solve this problem, we will use the Dirichlet boundary data:

$$\boldsymbol{u} = \boldsymbol{u}_D$$

If we now multiply by test functions $\boldsymbol{q} \in L^2(\Gamma_N)$ and integrate over the domain, we arrive to the equation:

$$\int_{\Gamma_D} \boldsymbol{q}(\boldsymbol{u} - \boldsymbol{u}_D)\ dS = 0$$

Now if we discretize both unknowns $\boldsymbol{u}$ and $\boldsymbol{\lambda}$ we can obtain the system of equations:

$$\left[\begin{array}{c|c} \boldsymbol{K} & \boldsymbol{A}^T \\ \hline \boldsymbol{A} & \boldsymbol{0} \end{array}\right] \left[\begin{array}{c} \boldsymbol{u} \\ \hline \boldsymbol{\lambda} \end{array}\right] = \left[\begin{array}{c} \boldsymbol{0} \\ \hline \boldsymbol{b} \end{array}\right]$$

If we now solve this linear system of equations, we can obtain $\boldsymbol{\lambda}$ and therefore the tractions $\boldsymbol{t}_N$ that we wanted to compute.