A large-strain poroelastic model for myocardial oedema formation

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1. INTRODUCTION

Poroelastic structures can be found in many biological applications, such as the study of biofilm growth distribution near fluids, cardiac perfusion and myocarditis formation (see Showalter (2005); Barnafi et al. (2021); Freitas Reis et al. (2019a)). This work concerns the formation of oedema, a build up of excess of fluid content in the myocardial intercellular space, due to an inflammatory reaction driven by the immune system.

We extend the results from Freitas Reis et al. (2019a,b) and develop a phenomenological model for the dynamic interaction between poroelastic finite-strain deformations and the chemotaxis of leukocytes towards pathogens. We address the local solvability of such model by studying its linearization, and additionally include the applicability of this model for large scale simulations by devising a robust block preconditioner (White et al. (2016)).

The main advantages of the proposed mathematical model and the associated computational methods are:

(1) a framework valid for finite strains,
(2) the versatility of the formulation to accommodate 2D or 3D geometries,
(3) the accuracy and efficiency of the numerical scheme,
(4) the potential of replacing invasive methods for the detection of interstitial fibrosis and myocarditis (such as endomyocardial biopsy) by techniques hinging only on MRI data.

2. THE MODEL

We consider an open connected domain Ω representing the heart that is deformed by a deformation field $\boldsymbol{x}$. A reference point $\boldsymbol{X}$ is deformed into the point $\boldsymbol{x}(\boldsymbol{X}, t) = \boldsymbol{X} + \boldsymbol{u}(\boldsymbol{X}, t)$, where $\boldsymbol{u}$ is the displacement field and $\boldsymbol{F} := \nabla \boldsymbol{x}$. The domain represents a mixture of extracellular and intracellular space, distributed according to their porosity, i.e. the local percentage of such phase pulled-back to reference configuration (MacMinn et al. (2016)), given respectively by ϕ, and $\phi_{\mathrm{IC}} = \det(\boldsymbol{F}) - \phi$. In the extracellular space we consider the concentration of the leukocytes and a pathogen, given by c_l and c_p respectively. These concentrations, together with the porosity, the pressure p acting on the intracellular space and the displacement form the main (primary) variables of our model.

The conservation of linear momentum is given by (MacMinn et al. (2016)):

$$-\operatorname{div}\left(\boldsymbol{P} - \alpha p \det(\boldsymbol{F})\boldsymbol{F}^{-T}\right) = \boldsymbol{0} \quad \text{in } \Omega,$$

where $\boldsymbol{P}$ is the Piola stress tensor, and α is the Biot-Willis modulus. The Piola stess tensor $\boldsymbol{P}$ is related to the primary variables through a Helmholtz potential Ψ such that $\boldsymbol{P} = \frac{\partial \Psi}{\partial \boldsymbol{F}}$, in our case given by the Holzapfel-Ogden energy (Holzapfel and Ogden (2009)).

In the extracellular space we consider the mass conservation of the liquid it contains, given by the following equation (MacMinn et al. (2016)):

$$\frac{d\phi}{dt} + \operatorname{div}\left(\phi \boldsymbol{K}(\boldsymbol{F}, \phi)\, \nabla\, p\right) = \Theta(p, c_p) \quad \text{in } \Omega,$$

where $\boldsymbol{K}$ is modeled with an isotropic power law, and the immune response is modeled through Θ using a Starling-Hill function (Freitas Reis et al. (2019a)). The evolution of the immune system dynamics related to the concentrations c_p, c_l is dictated by the following mass conservation laws:

$$\frac{d(\phi c_p)}{dt} - \operatorname{div}\left(\phi \boldsymbol{D}_p(\boldsymbol{F}) \nabla c_p\right) = r_p(\phi, c_p, c_l), \quad \text{in } \Omega,$$

$$\frac{d(\phi c_l)}{dt} - \operatorname{div}\left(\phi \boldsymbol{D}_l(\boldsymbol{F}) \nabla c_l - \chi \phi c_l \nabla c_p\right) = r_l(\phi, c_p, c_l), \quad \text{in } \Omega.$$

both valid throughout Ω, where $\boldsymbol{D}_p, \boldsymbol{D}_l$ are the pulled-back diffusion tensors for the species in the extracellular space, χ is the leukocyte chemotactic rate and r_p, r_l are the reaction terms that yield the interaction between the pathogen and the leukocytes. The last equation is given by the incompressibility of the intracellular space:

$$\det(\boldsymbol{F}) - \phi = 1 - \phi_0, \quad \text{in } \Omega,$$

where ϕ_0 represents the initial (resting) porosity.

3. RESULTS

In Figure 1 we show the evolution of the chemotaxis variables c_p (first row) and c_l (second two), where it can be appreciated how leukocytes appear as a reaction to the passage of the pathogen.

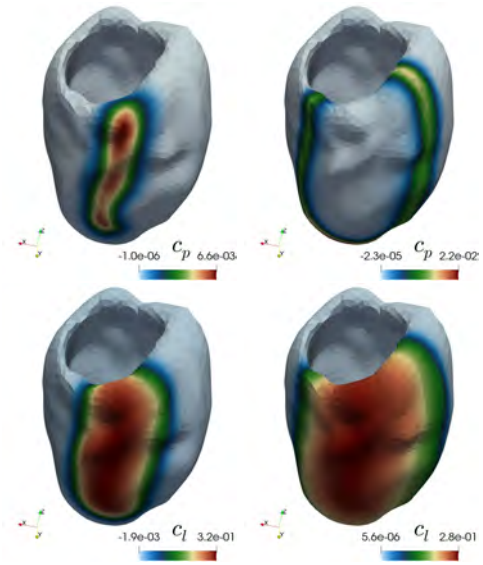

Fig. 1. Evolution of pathogens and leukocytes concentration (first and second row, respectively) at $t = 0$ minutes and $t = 15$ minutes.

In our work we report five different numerical tests: i) a sensitivity analysis, where pathogen concentration, pressure and displacement were studied for a wide range of different parameters; ii) an isolated poromechanics study, where compression and drainage responses of the tissue were verified; iii) a coupled chemotaxis study, where the entire model was tested with an initial concentration of pathogen in a 2D square domain; iv) a convergence study, to validate the approximability properties of our proposed numerical scheme; lastly, v) an integrated simulation in a real left ventricle geometry, together with a verification of the robustness of our preconditioner in such case.

4. CONCLUSIONS

We have proposed a general model capturing the phenomenological features of the interaction between chemotaxis of the immune system in saturated poroelastic media admitting large deformations. The problem exhibits a saddle-point structure that allowed us to devise an adequate approximation scheme, that we complemented with a block-partitioned preconditioner. The vast collection of numerical tests allow us to conclude that our model yields a physiologically accurate behavior, which together with our scalable solver results in a realistic model that can be efficiently approximated numerically in large scale simulations.

Further investigation is necessary, for instance, regarding the specific role of the anisotropic porous structure of the tissue, as well as in designing new coupling mechanisms that will contribute to a better understanding of the formation and termination of myocarditis and myocardial oedema. Another fundamental problem to address is that of a more thorough sensitivity analysis, in order to better understand the role of each of the many parameters involved in the model, so that they can be more easily adapted to patient-specific scenarios.

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