Multiscale modeling of calcified hydrogel networks

Serhat Aygün1,* and Sandra Klinge1

1 Chair of Structural Mechanics and Analysis, TU Berlin, Straße des 17. Juni 135, 10623 Berlin, Germany

The model proposed simulates the effective material behavior of calcified hydrogels using the multiscale finite element method (FEM). To this end, representative volume elements (RVEs) are generated to depict the biphasic material microstructure consisting of the organic hydrogel and inorganic calcium phosphate. The choice of the hydrogel matrix influences the type of agglomeration of the inorganic phase and thus dictates the geometry of the RVE. Most commonly, the inorganic phase appears in the form of spherical inclusions or honeycomb grids where the characteristic size of a typical unit may vary. The approach proposed treats the calcified regions as Neo-Hookean material and assumes the Ogden model for the hydrogel. The contribution closes with the numerical results on the effective material behavior and their validation with respect to experimental findings.

© 2021 The Authors. Proceedings in Applied Mathematics & Mechanics published by Wiley-VCH GmbH.

1 Introduction

Hydrogels are cross-linked 3D networks of polymer chains that do not dissolve in water but are able to absorb it. Their ability to absorb water goes back to the presence of hydrophilic functional groups that are attached to the polymeric backbone, whereas cross-links between network chains yield the resistance to dissolution [1]. Hydrogels already have a large application spectrum and can be used in agriculture, sealing, coal dewatering, additives, etc. They also have great potential to be used for biomedical purposes such as tissue engineering, drug delivery, self-healing materials, biosensors, and hemostasis bandages. Compared to other types of biomaterials, hydrogels show some important advantages: increased biocompatibility, tunable biodegradability, proper mechanical strength and porous structure [2]. In spite of this, the improvement of the material strength and ductility are still open topics strongly motivating the further investigation of new types of synthetic materials with a tunable microstructure and customized functionality.

The present work studies amorphous calcium phosphate nanostructures in polymer hydrogels which are generated by using the enzyme-induced mineralization. This process leads to synthetic ultrastable hydrogels with high toughness, both in their dry state and when swelling in water. The calcification process forms various shapes of inclusions depending on the choice of the underlying matrix polymer. For example, the network of PDMA-l-TEG contains spherical porous structures of the inorganic component calcium phosphate, whereas PAAm-l-MBAm forms a honeycomb-like structure [3].

2 Mechanical modeling of calcified hydrogels

The concept of multiscale FEM enables to capture the influence of a two-phasic microstructure on the effective behavior of hydrogels. To this end, the geometry of the RVE and constitutive laws for single phases have to be proposed. The current model assumes the Ogden material for modeling the nonlinear behavior of hydrogels. In this case, free energy of the hydrogel $\Psi_{\text{hyd}}$ is split into volumetric part $U$ and scalar deviatoric function $W$

$$\Psi_{\text{hyd}}(J, \lambda_A^{\text{dev}}) = K_{\text{hyd}} U(J) + \sum_{A=1}^{3} W(\lambda_A^{\text{dev}}), \quad U(J) = \frac{1}{4} (J^2 - 1 - 2 \ln(J)), \quad W(\lambda_A^{\text{dev}}) = \sum_{j=1}^{3} C_j (\lambda_A^{\text{dev}})^{\alpha_j} (\lambda_A^{\text{dev}})^{-1}.$$

where $J = \det(F)$ represents the determinant of the deformation gradient $F$, $K_{\text{hyd}}$ is the bulk modulus of the hydrogel and $\lambda_A^{\text{dev}} = J^{-\frac{1}{3}} \lambda_A$ are deviatoric parts of principal stretches $\lambda_A$. Furthermore, $C_j$ and $\alpha_j$ are the constants of the Ogden model. The modeling of the second phase, calcium phosphate, assumes the Neo-Hookean model with free energy $\Psi_{\text{cal}}$

$$\Psi_{\text{cal}} = \left( K_{\text{cal}}^{\text{2/3}} \right) U(J) + \frac{1}{2} G (I_1 - 3 - 2 \ln(J)), \quad I_1 = \sum_{A=1}^{3} \lambda_A,$$

where $K_{\text{cal}}$ is the bulk modulus of the calcium phosphate, $G$ is the shear modulus and $I_1$ is the first invariant.

In a further step, the multiscale finite element method is used to simulate the effective behavior of a network of calcified hydrogels. According to this concept, the original problem of modeling a structure with the heterogeneous microstructure is replaced by two boundary-value problems (BVPs). One of these BVPs is related to the macroscopic (structural) level, whereas...

* Corresponding author: e-mail serhat.aygun@tu-dortmund.de

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
the other one simulates the RVE behavior. The interaction of results at different scales is dictated by the macrohomogeneity Hill-Mandel condition on the energy balance at a material point [4]

\[
P : \bar{\mathbf{F}} = \frac{1}{V} \int_B P : \mathbf{F} dV \quad \Rightarrow \quad \frac{1}{V} \int_B (\mathbf{t} - P N) \cdot (\mathbf{x} - \bar{\mathbf{F}} X) dA = 0.
\]

Here, \( P \) is the first Piola-Kirchhoff stress tensor, \( \mathbf{F} \) the deformation gradient, \( \mathbf{t} \) the traction, \( N \) the normal vector to the surface and \( B \) the RVE with the volume \( V \). According to the notation typical for the theory of finite deformations, capital letters denote quantities related to the reference configuration, and lower case letters represent quantities related to the current configuration. The overbar symbol denotes the macroscopic quantities.

3 Numerical simulation of calcified hydrogels

Chosen numerical examples simulate macroscopic tensile tests on a square sample with dimensions of 10 mm \( \times \) 10 mm. The lower boundary is constrained and a gradually increasing vertical force within the range \([0, 1 \, \text{N}]\) is applied at the upper boundary. Remaining boundaries are not constrained. In order to depict different microstructures, two RVEs are chosen (Figs. 1a and b). They include two phases: hydrogel matrix (blue color) and the calcium phosphate (grey color). The honeycomb-like structure of the inorganic phase is typical of PDMA-l-TEG (Fig. 1a), whereas the spherical structure appears in the PDMA-l-TEG (Fig. 1b). Simulations assume elasticity coefficients for hydrogels as proposed by Takigawa et al. [5], whereas remaining material constants are fitted to the experimental results shown in [3]. The simulation results agree excellently with the experimental data and indicate that the PAAm-l-MBAm has a higher stiffness compared to PDMA-l-TEG. This goes back to the material properties of the matrix material as well as to the geometry and volume fraction of phases.

Fig. 1: (a) The RVE with honeycomb-like structure of calcium phosphate. (b) The RVE with spherical structure of calcium phosphate. (c) Comparison of numerical results for the stress-strain curve with experimental data [3]. The applied material parameters: \( K^{\text{cal}} = 46 \, \text{MPa} \), \( G = 50 \, \text{MPa} \), \( K^{\text{PAAm}} = 33 \, \text{MPa} \), \( K^{\text{PDMA}} = 20 \, \text{MPa} \), \( C_1 = 0.08 \, \text{MPa} \), \( \alpha_1 = 5 \), \( C_2 = 1.5 \, \text{MPa} \), \( \alpha_2 = 1 \), \( C_3 = 10 \, \text{MPa} \), \( \alpha_3 = 2 \).

4 Conclusions

The present contribution shows the applicability of the multiscale FEM for the prediction of the effective material behavior of calcified hydrogels. These biphasic materials consist of an organic phase (hydrogel) and an anorganic phase (calcium phosphate) and show significant differences in the microstructure form. PDMA-l-TEG and PAAm-l-MBAm hydrogels are used as illustrative examples and numerical results achieved show an excellent agreement with the experimental observations. This highly substantiates the simulation of alternative hydrogel combinations as well as the investigation of their properties with the regard to damage and ductility.

Acknowledgements We gratefully acknowledge the financial support by the German Research Foundation (DFG) for the scientific project KL 2678/10-1. Open access funding enabled and organized by Projekt DEAL.

References

[1] E. M. Ahmed, Hydrogel: Preparation, characterization, and applications: A review, J. Adv. Res. 6 (2), 105–121, 2015.
[2] C. Qinyuan, J. Yang, and Y. Xinjun, Hydrogels for biomedical applications: Their characteristics and the mechanisms behind them, Gels 3 (1), 3010006, 2017.
[3] N. Rauner, M. Meuris, M. Zoric, and J. C. Tiller, Enzymatic mineralization generates ultrastiff and tough hydrogels with tunable mechanics, Nature 543, 407–410, 2017.
[4] S. Klinge, S. Aygün, R. P. Gilbert, and G. A. Holzapfel, Multiscale FEM simulations of cross-linked actin network embedded in cytosol with the focus on the filament orientation, Int. J. Numer. Method Biomed. Eng. 34 (7), e2993, 2018.
[5] T. Takigawa, Y. Morino, K. Urayama, and T. Masuda, Poisson’s ratio of polyacrylamide (PAAm) gels, Polym. Gels Networks 4 (1), 1–5, 1996.

© 2021 The Authors. Proceedings in Applied Mathematics & Mechanics published by Wiley-VCH GmbH.