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Stiffness and Strength Prediction for a Hydroxyapatite-Based Biomaterial, Considering Bone Regeneration

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Introduction

Bone tissue engineering scaffolds must blend in the targeted physiological environment, i.e. the immediate vicinity of bone tissue, as well as possible [1,2]. From a mechanical perspective, careful tuning of such scaffold structures (and of the underlying materials) is necessary because **scaffold structures must be stiff enough** to sustain all relevant mechanical load cases, **but also soft enough** to facilitate, through mechanobiological couplings [3], the integration into their bony environment. Two mechanical properties are of particular interest, namely the **stiffness and the strength**.

In this work, we study one specific scaffold material that has been developed as bone replacement material with the human mandible as targeted application area [4,5]. This biomaterial is produced in form of **porous, pre-cracked granules, composed of hydroxyapatite as main constituent, but also including various kinds of pore spaces** of distinctively different characteristic lengths.

After exposing this biomaterial to the targeted physiological environment prevailing in the immediate vicinity of mandibular bone tissue, two mechanisms are triggered, causing a progressing change of the material's composition over time. On the one hand, bone tissue grows on the granule surfaces, while, on the other hand, concurrently the hydroxyapatite crystals are resorbed - in the long run, the scaffold material merges with the surrounding bone tissue.

For analyzing the mechanical behavior of the granules, we present a **three-step, fully continuum micromechanics-based model**, allowing, on the one hand, for **upscaling of the material's stiffness**, and, on the other hand, for downscaling of stresses and strains applied macroscopically, linking in the end the quasi-brittle failure of single micrometer- or sub-micrometer-sized hydroxyapatite crystal needles to the **overall strength of both millimeter-sized biomaterial scaffolds and composites** comprising biomaterial scaffold and bone tissue, respectively.

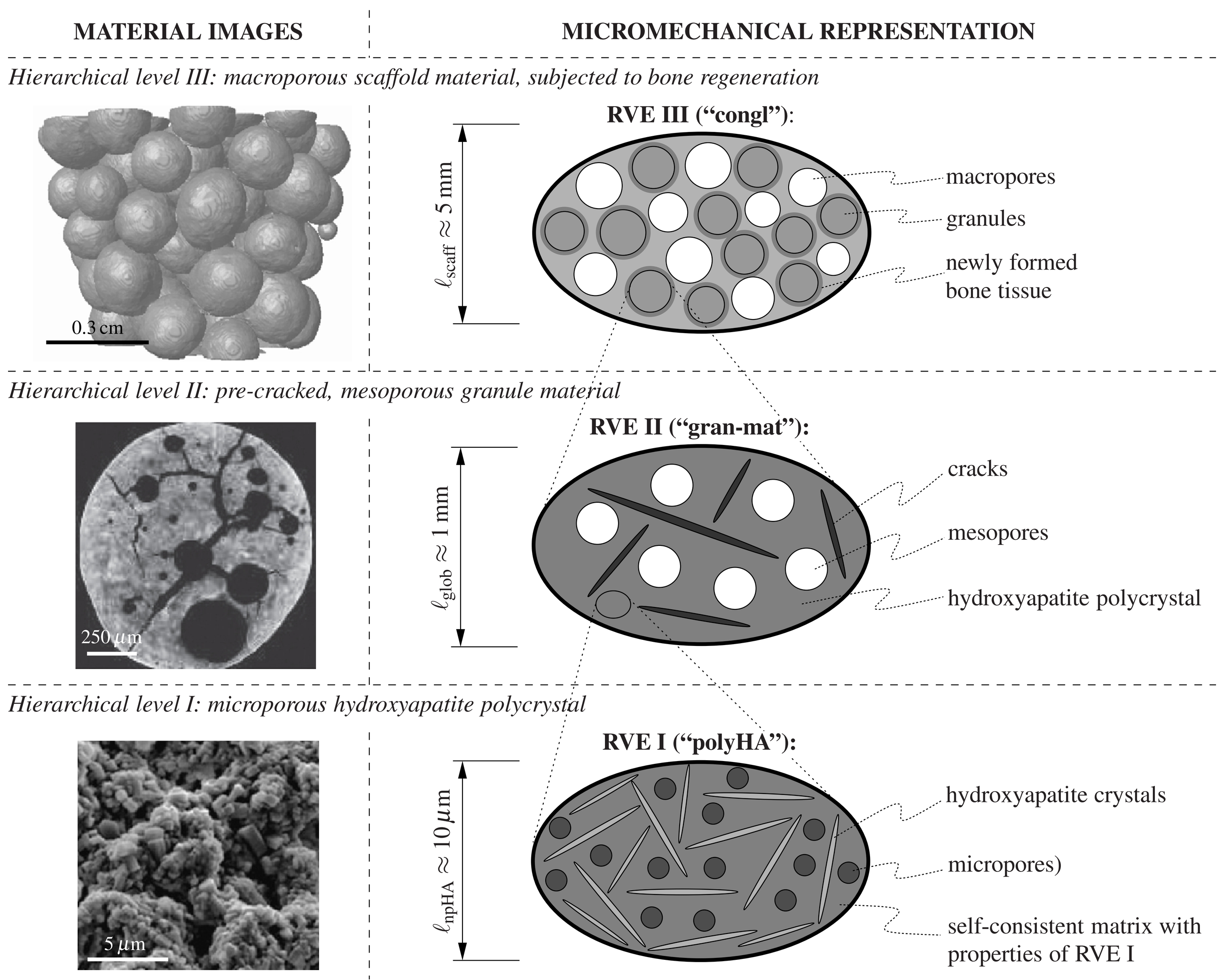
Materials and Methods

Definition of the material

- Granular scaffold material, composed of carbonate containing hydroxyapatite
- Composition: $Ca_{10}(PO_4)_6(OH)_{1.9}(CO_3)_{0.05}$
- Production makes use of the effect of immiscible fluids [4,5]
- Diameters range from 0.05 to 2 mm

Image of the studied biomaterial when placed in the targeted physiological environment, i.e. the immediate vicinity of mandibular bone tissue

Material hierarchy and multiscale model representation



Left column: hierarchical organization of the studied biomaterial; right column: corresponding three-level model representation, complying with the requirement of separated scales [6-8], being the basis for micromechanics-based stiffness and strength estimation

Modeling strategy

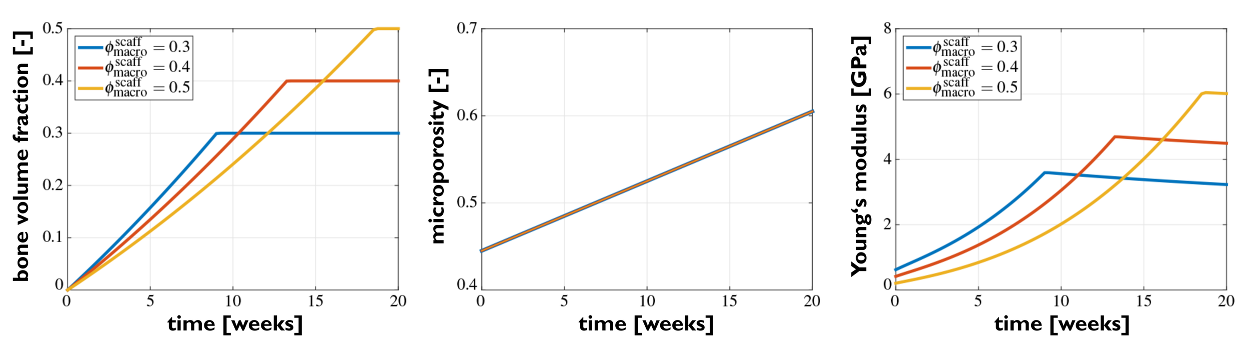
Employed concept: continuum micromechanics [6-8]

- Macrohomogeneous, but microheterogeneous **representative volume elements (RVEs)** are introduced, fulfilling the "separation of scales"-requirement, $d \ll \ell$
- Quasi-homogeneous subdomains, so-called **material phases**, with known physical properties, are chosen within the RVE
- On hierarchical levels I and II, **classical micromechanical homogenization schemes** are utilized for stiffness estimation [9,10]
- On hierarchical level III, additionally, **hydrostatic and pure shear displacement boundary value problems** are solved, for computing the macroscopic stiffness tensor $\mathbb{C}_{\text{scaff}}$ [11]
- Prescribing an **quasi-brittle failure criterion for the hydroxyapatite needles** allows for estimation of the ultimate macroscopic load $\Sigma^{\text{ult}}_{\text{scaff}}$ [12]
- Bone ingrowth is considered based on the bone ingrowth rate k_{growth}, following from histological studies
- Scaffold dissolution is considered based on the scaffold resorption rate k_{res}, following from dissolution studies

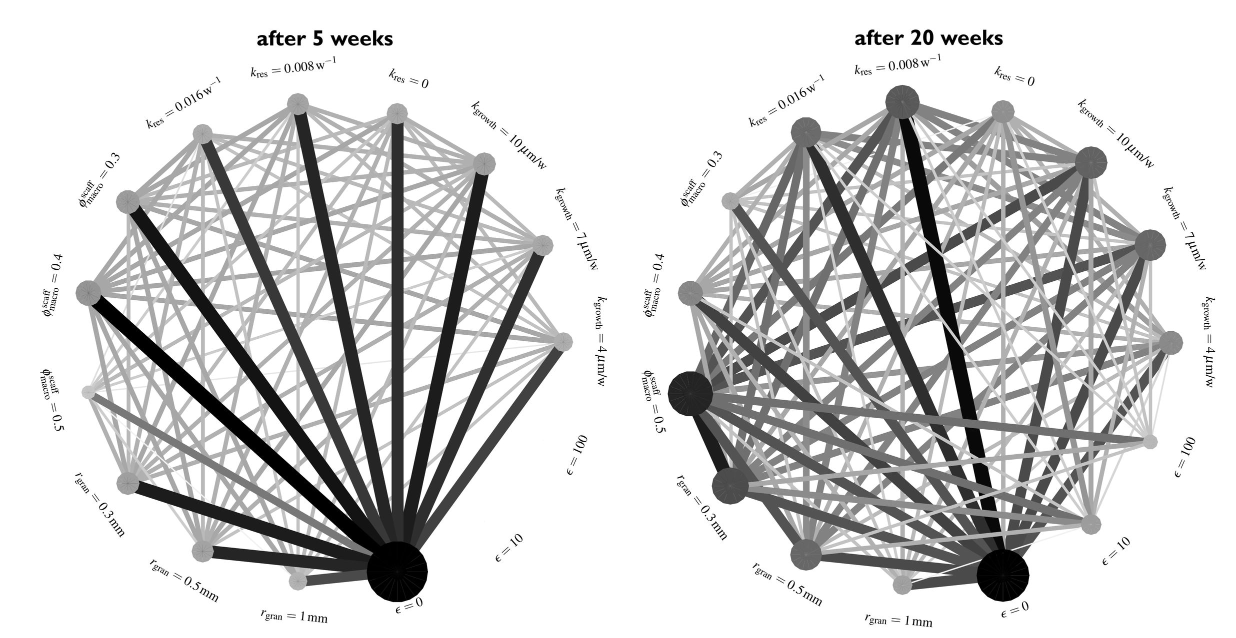
Numerical Results

Stiffness estimation

- Model allows for efficient assessment of the effects of design parameters on stiffness development
- The low crack density is crucial for an adequate stiffness
- A high macroporosity allows for reaching high stiffness, as enough space for bone ingrowth is provided
- The granule radius should be small, as the stiffness increase due to bone ingrowth is faster than for large granules
- Scaffold resorption rate and bone ingrowth rate appear to be equally important



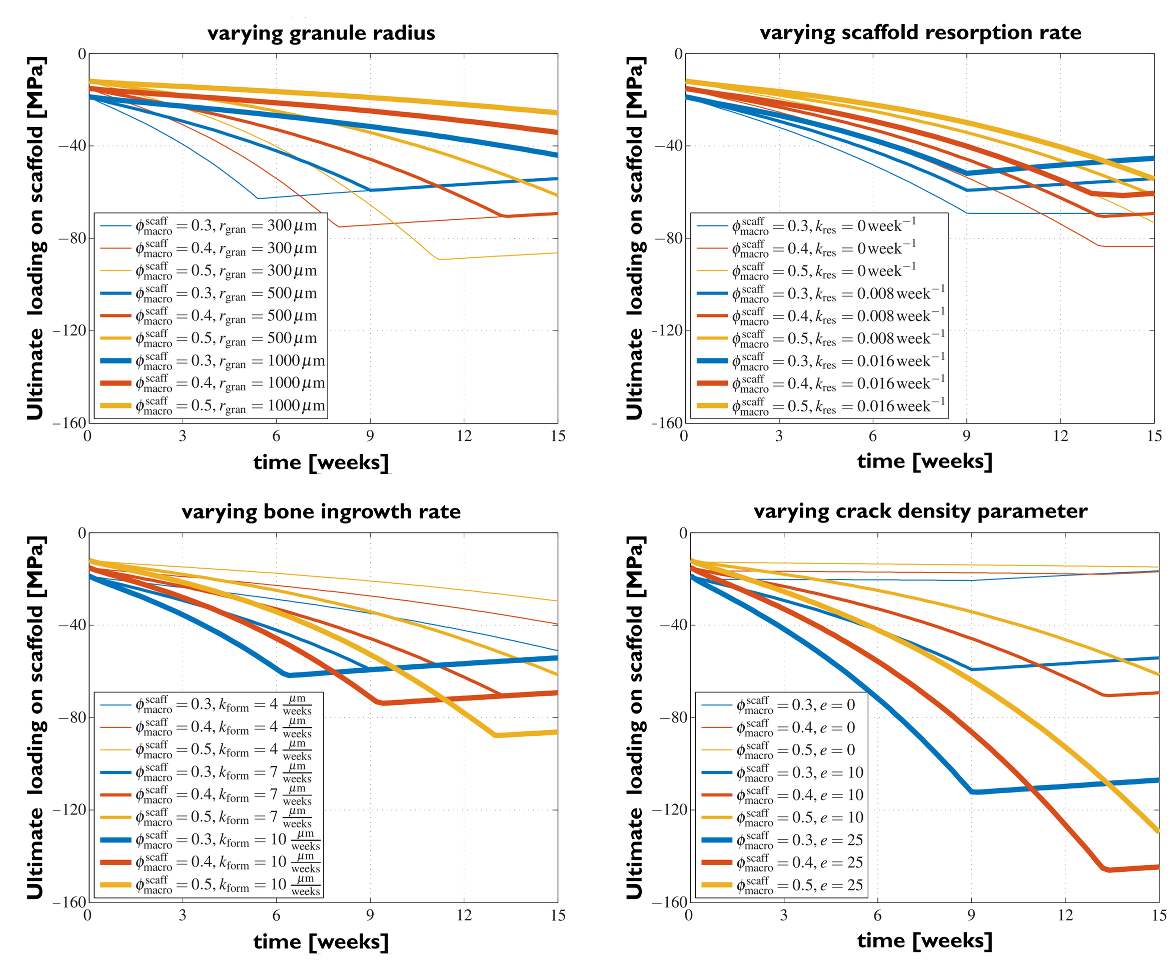
Model-predicted evolutions of bone volume fraction, microporosity, and corresponding Young's modulus over time, for fixed granule radius (0.5 mm), fixed mesoporosity (0.189), fixed crack density parameter (10), fixed resorption rate (0.008 week^{-1}), and fixed bone growth rate (7 mm/week)



Parameter combinations that yield an adequate, model-predicted Young's modulus, i.e. between 5 and 19 GPa; the circle size is indicative for the importance of single parameters, the line thickness is indicative for specific parameter combinations

Strength estimation

- Smaller granule radii lead to a faster strength increase, due to faster bone ingrowth
- The scaffold resorption rate particularly influences the long-term development of strength
- The bone ingrowth rate particularly influences the short-term development of strength
- Strength estimates are directly proportional to the crack density since uncracked granules attract more stress than cracked ones



Influence of parameter variations on the model-predicted ultimate loading of the scaffold material

Future model improvements:

- Introduction of adequate failure criteria for the bone tissue, to improve strength predictions
- Coupling of the mechanical model with systems biology models, to take into account the influence of the biological environment of the scaffold material

References and Acknowledgments

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