Mathematical Modeling Employed for Biomaterials Design

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Vienna University of Technology, Austria

COST MP1301: New generation biomimetic and customized implants for bone engineering

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Sofia, Bulgaria

Motivation

MOTIVATION

FUNDAMENTAL INTRICACY OF BIOMATERIALS DESIGN:

- must be **stiff enough** to provide the required load carrying-capacity
- must **blend in physiological environment**
- and **facilitate biological processes**, granted by
  - ➡ sufficient porosity, allowing for distribution of biological factors
  - ➡ sufficient „softness“, allowing for adequate mechanical stimulation of biological processes

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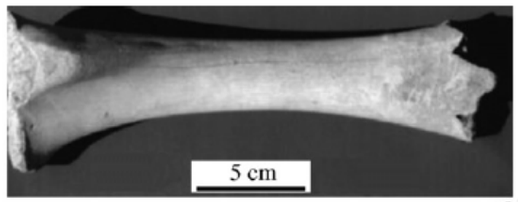
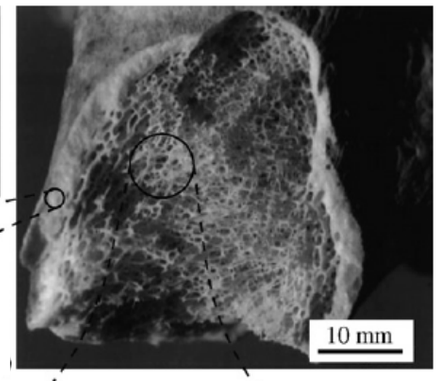
ULTIMATE GOAL OF RELATED RESEARCH AT IMWS:

- development of mathematical models allowing for **prediction of the mechanical properties** of biological tissues and biomaterials
- taking into account the **materials' composition** and the available **microstructural information**
- utilizable for both **material design and assessment**

Hierarchical organization of Bone

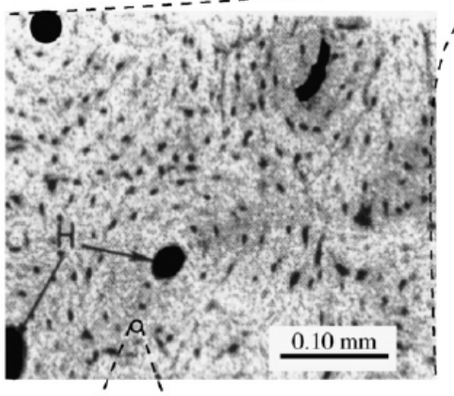
whole long bone

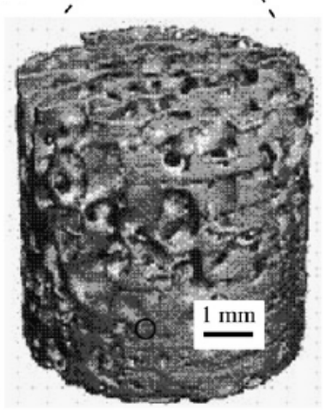




cross section of long bone

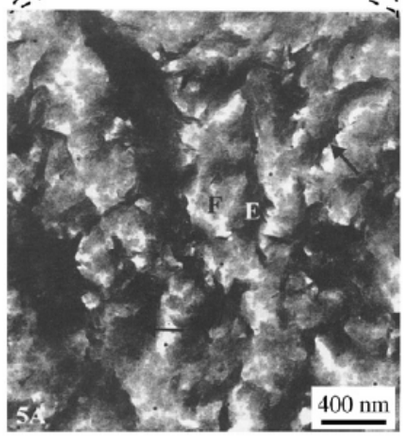
cortical bone

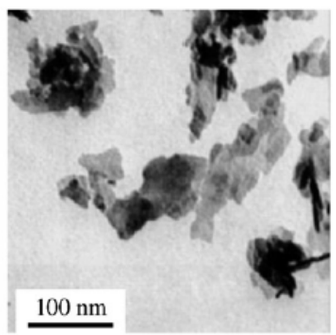




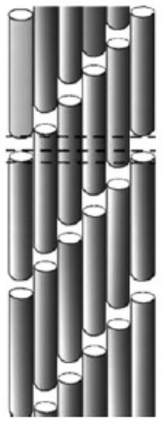
trabecular bone

extracellular bone matrix





hydroxyapatite crystals



collagen molecules

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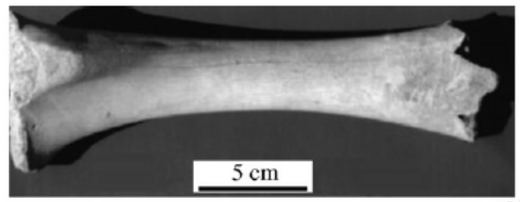

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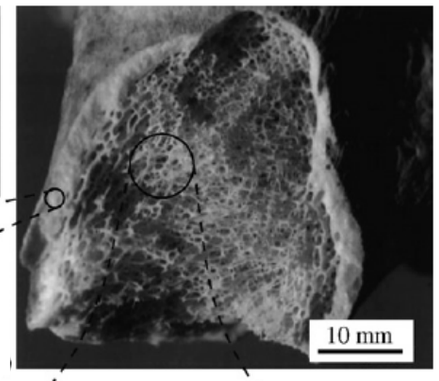

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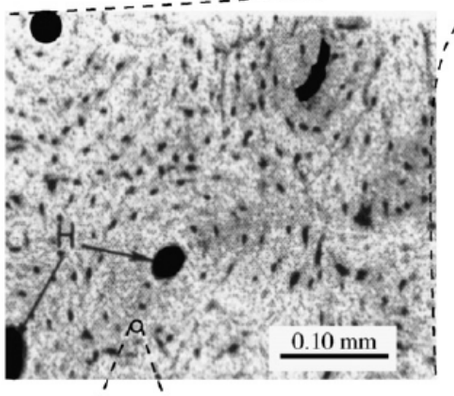

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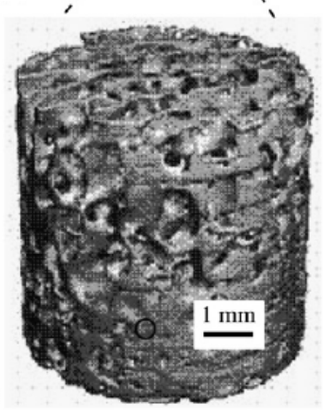

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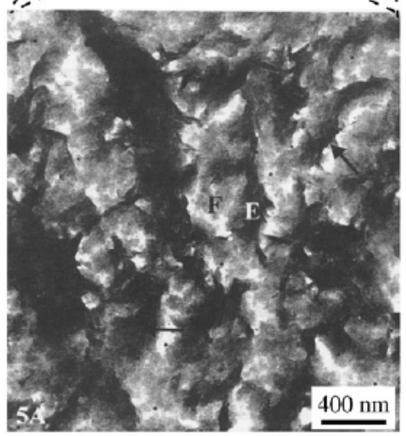

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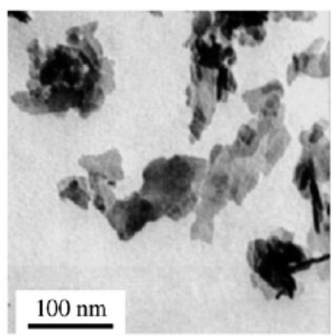

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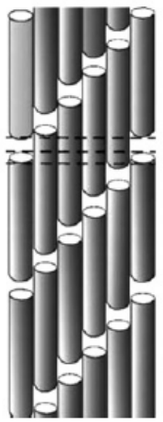

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- Adequate **computation** of the **mechanical properties** on the macroscopic scale requires **thorough, reasonable, and efficient integration of relevant information** available on lower observation scales

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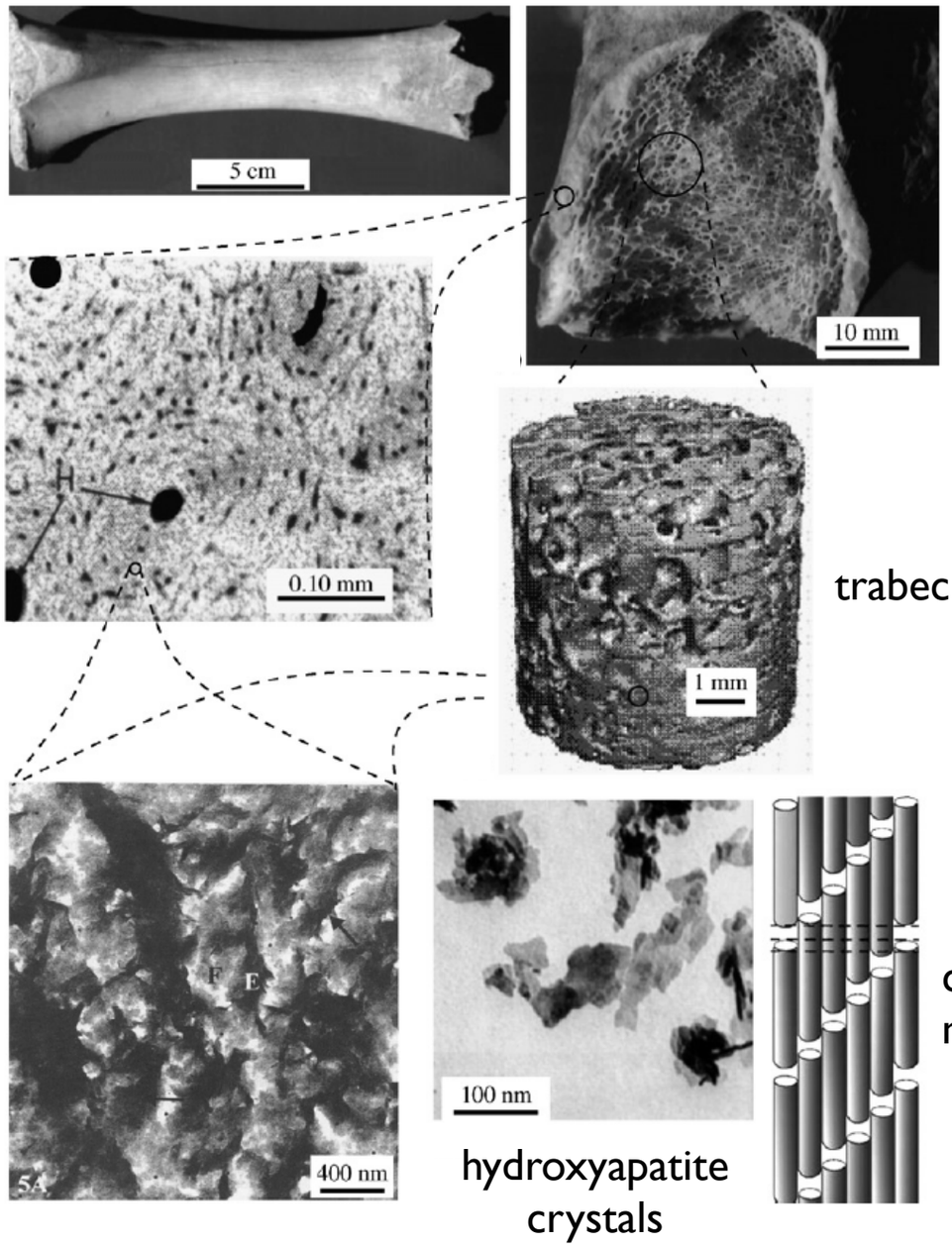

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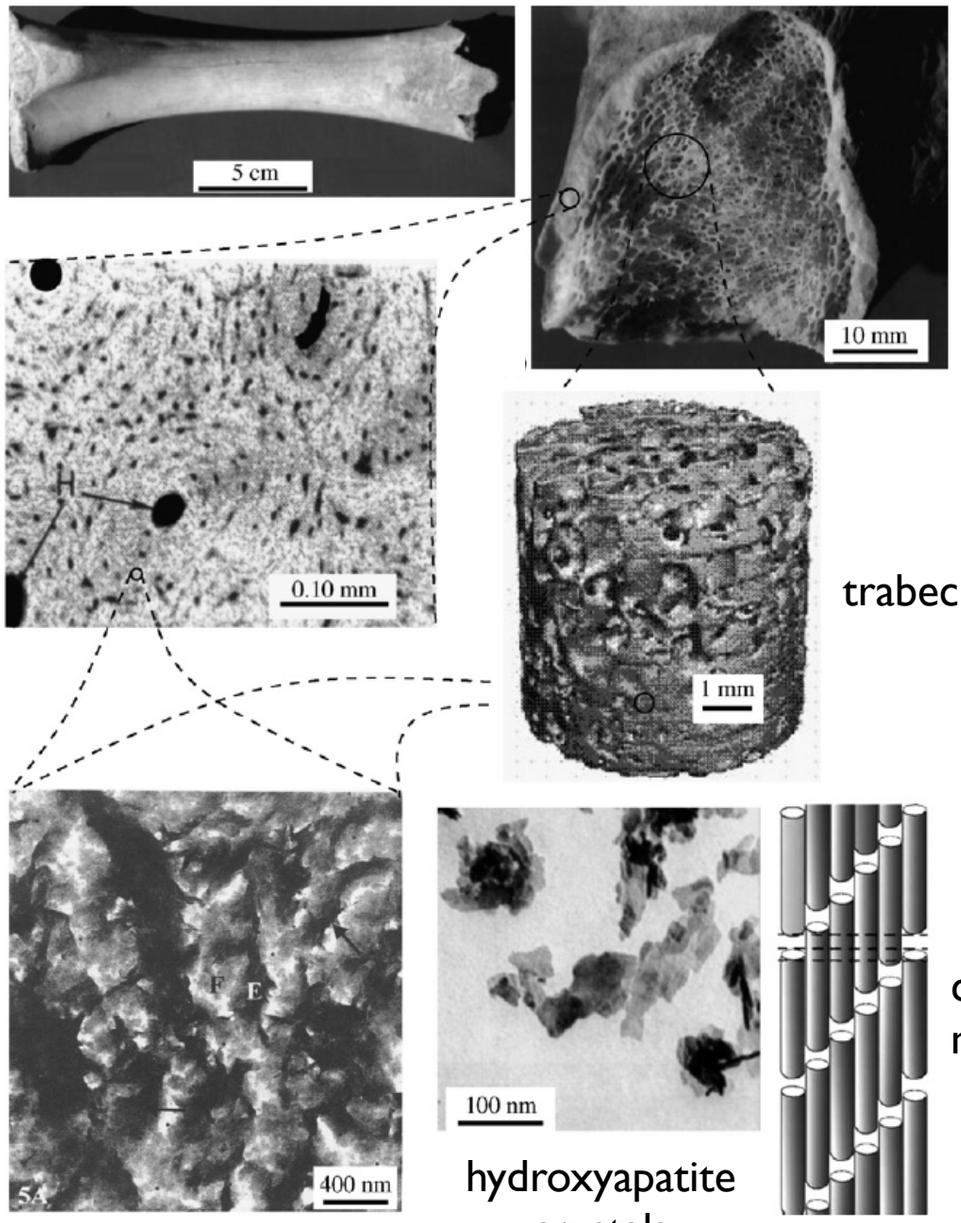

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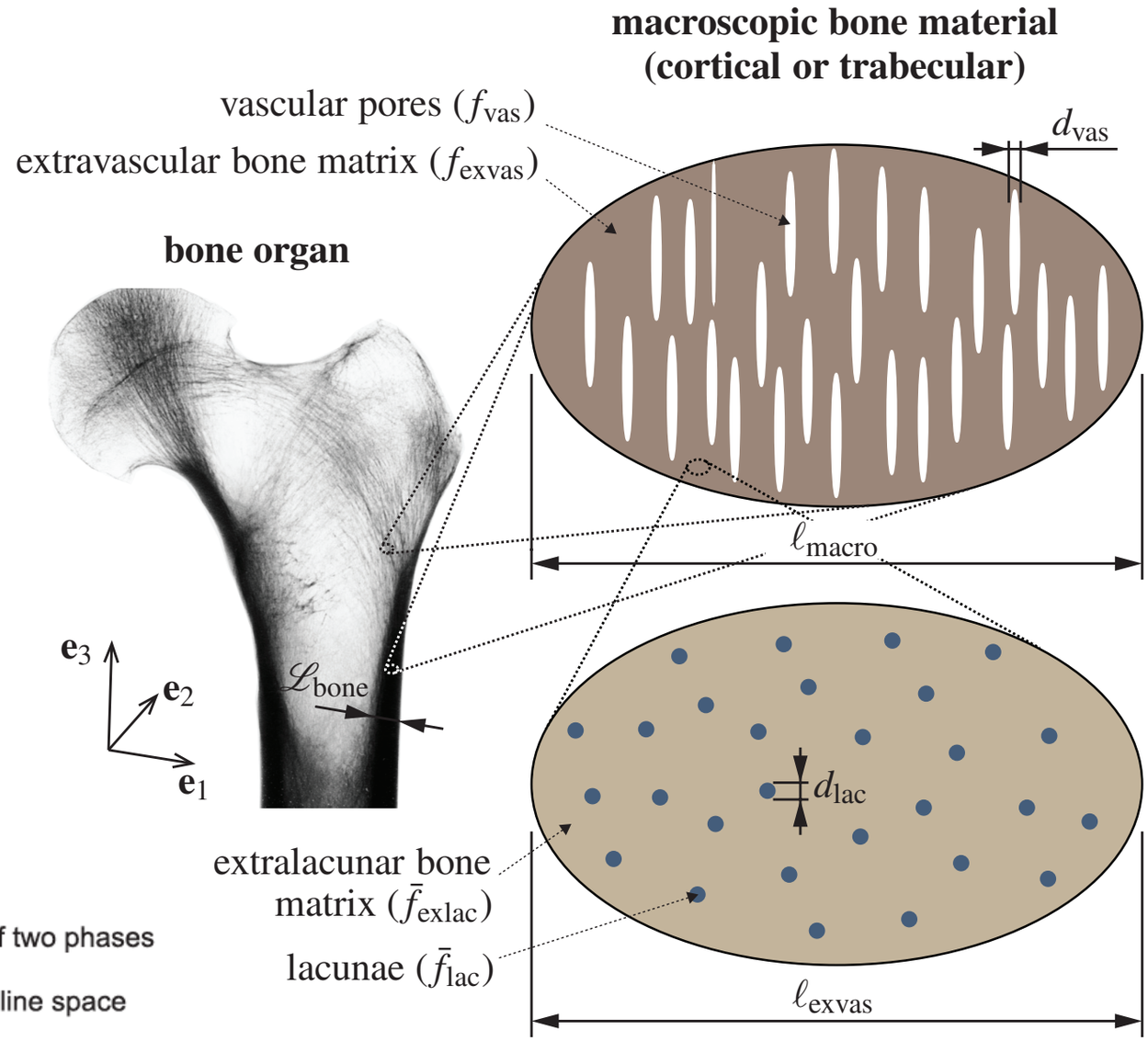
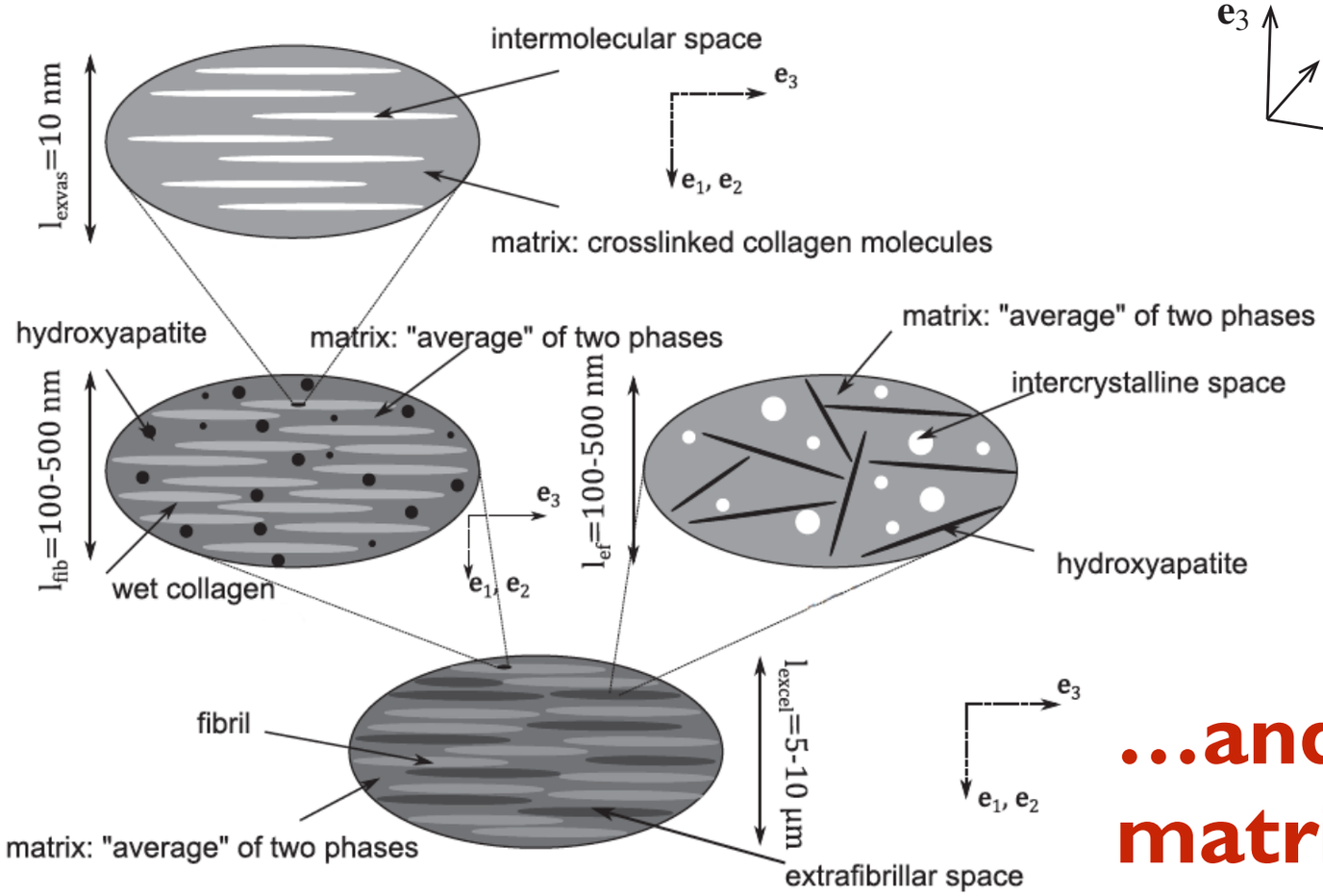
- **Efficient and physically coherent** alternative method: **continuum micromechanics**-based homogenization methods

Micromechanical Representation of Bone

From bone organ to extracellular (or -lacunar) bone matrix…





…and from extracellular bone matrix to collagen molecules

see e.g. Hellmich and Ulm (2002), *Journal of Engineering Mechanics (ASCE)* 128: 898-908; Fritsch and Hellmich (2007), *Journal of Theoretical Biology* 244: 597-620; Vuong and Hellmich (2011), *Journal of Theoretical Biology* 287: 115-130; Morin and Hellmich (2015), *Ultrasonics* 54: 1251-1269; Scheiner et al., *Biomechanics and Modeling in Mechanobiology*, available online

Prediction of Bone Stiffness

Fritsch and Hellmich (2007), *Journal of Theoretical Biology* 244: 597-620

Prediction of Bone Stiffness

Required input: stiffness of „basic building blocks“

➡ stiffnesses of **hydroxyapatite**, **water**, and **collagen** are provided by experimental studies (in terms of bulk and shear moduli, and stiffness tensor components)

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Five-step homogenization scheme for „scaling“ the stiffness tensors from the collagen level up to the extravascular level:

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$$\mathbb{C}_{wetcol}^{MT} = \{(1-\mathring{f}_{im})\mathbb{c}_{col} + \mathring{f}_{im}\mathbb{c}_{im} : [\mathbb{I} + \mathbb{P}_{cyl}^{col} : (\mathbb{c}_{im} - \mathbb{c}_{col})]^{-1}\}$$
$$: \{(1-\mathring{f}_{im})\mathbb{I} + \mathring{f}_{im}[\mathbb{I} + \mathbb{P}_{cyl}^{col} : (\mathbb{c}_{im} - \mathbb{c}_{col})]^{-1}\}^{-1}$$

$$\mathbb{C}_{ef}^{SCSII} = \left\{ \sum_r \check{f}_r \, \mathbb{c}_r : [\mathbb{I} + \mathbb{P}_{sph}^{ef} : (\mathbb{c}_r - \mathbb{C}_{ef}^{SCSII})]^{-1} \right\}$$
$$: \left\{ \sum_s \check{f}_s [\mathbb{I} + \mathbb{P}_{sph}^{ef} : (\mathbb{c}_s - \mathbb{C}_{ef}^{SCSII})]^{-1} \right\}^{-1}$$

$$\mathbb{C}_{fib}^{SCS}$$
$$= \{\check{f}_{wetcol}\, \mathbb{C}_{wetcol}^{MT} : [\mathbb{I} + \mathbb{P}_{cyl}^{fib} : (\mathbb{C}_{wetcol}^{MT} - \mathbb{C}_{fib}^{SCS})]^{-1}$$
$$+ \check{f}_{HA}\, \mathbb{c}_{HA} : [\mathbb{I} + \mathbb{P}_{sph}^{fib} : (\mathbb{c}_{HA} - \mathbb{C}_{fib}^{SCS})]^{-1}\}$$
$$: \{\check{f}_{wetcol}[\mathbb{I} + \mathbb{P}_{cyl}^{fib} : (\mathbb{C}_{wetcol}^{MT} - \mathbb{C}_{fib}^{SCS})]^{-1}$$
$$+ \check{f}_{HA}[\mathbb{I} + \mathbb{P}_{sph}^{fib} : (\mathbb{c}_{HA} - \mathbb{C}_{fib}^{SCS})]^{-1}\}^{-1}$$

$$\mathbb{C}_{ultra}^{MTII} = \{(1-\bar{f}_{fib})\mathbb{C}_{ef}^{SCSII} + \bar{f}_{fib}\mathbb{C}_{fib}^{SCS} : [\mathbb{I} + \mathbb{P}_{cyl}^{ef}$$
$$: (\mathbb{C}_{fib}^{SCS} - \mathbb{C}_{ef}^{SCSII})]^{-1}\} : \{(1-\bar{f}_{fib})\mathbb{I} + \bar{f}_{fib}[\mathbb{I} + \mathbb{P}_{cyl}^{ef}$$
$$: (\mathbb{C}_{fib}^{SCS} - \mathbb{C}_{ef}^{SCSII})]^{-1}\}^{-1}$$

$$\mathbb{C}_{exvas}^{MTIII} = \{\tilde{f}_{ultra}\mathbb{C}_{ultra}^{MTII} + \tilde{f}_{lac}\, \mathbb{c}_{lac} : [\mathbb{I} + \mathbb{P}_{sph}^{ultra} : (\mathbb{c}_{lac} - \mathbb{C}_{ultra}^{MTII})]^{-1}\}$$
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Five-step homogenization scheme for „scaling“ the stiffness tensors from the collagen level up to the extravascular level:

based on…

- aforementioned **component-specific stiffnesses**
- volume fractions of the components quantifying the **composition of the bone tissue**
- **phase shapes and morphologies** (taken into account through Hill tensors)

Fritsch and Hellmich (2007), *Journal of Theoretical Biology* 244: 597-620

Prediction of Bone Stiffness

Model validation based on comparison with **independent** experimental data:

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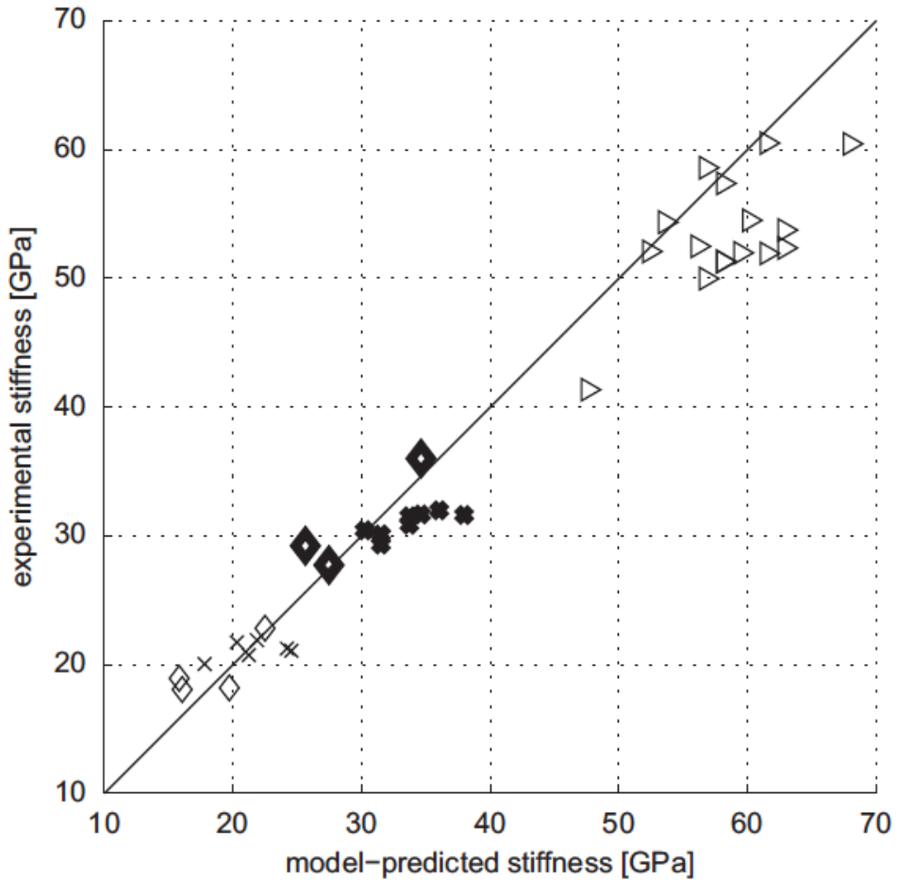
Prediction of Bone Stiffness

Model validation based on comparison with **independent** experimental data:

on the extracellular level



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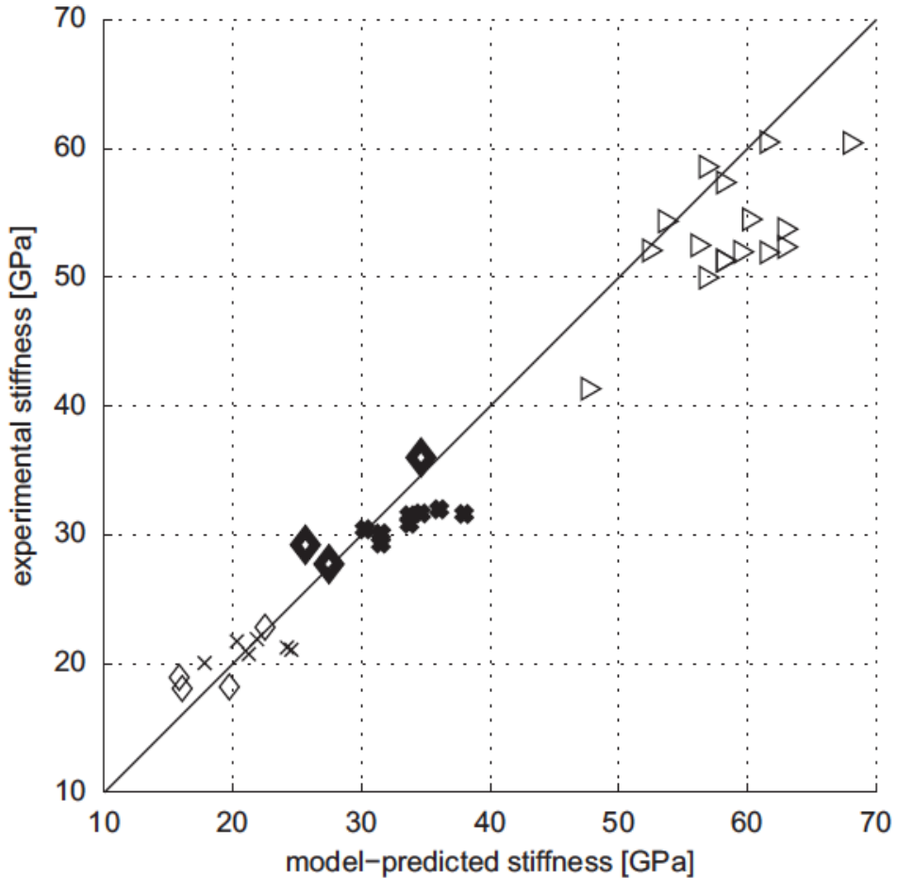

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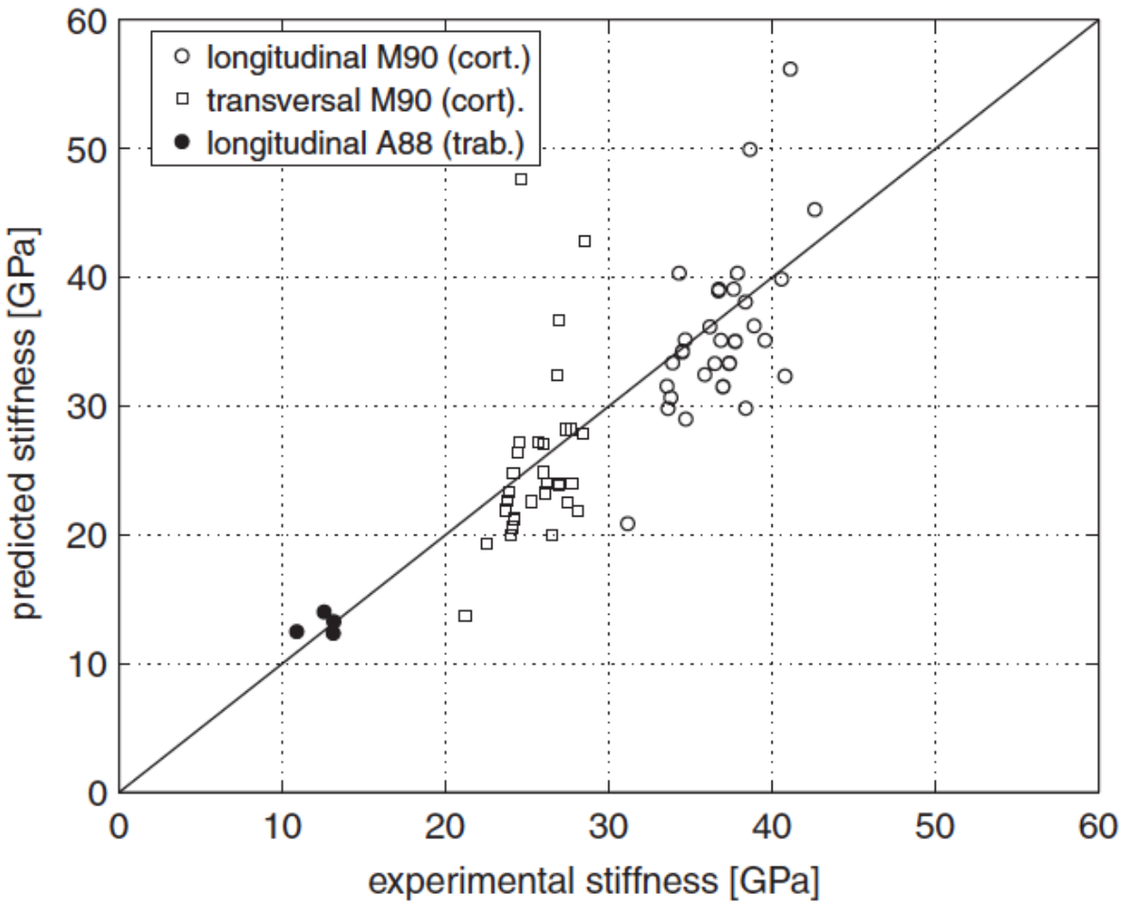

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Prediction of Further Bone Properties

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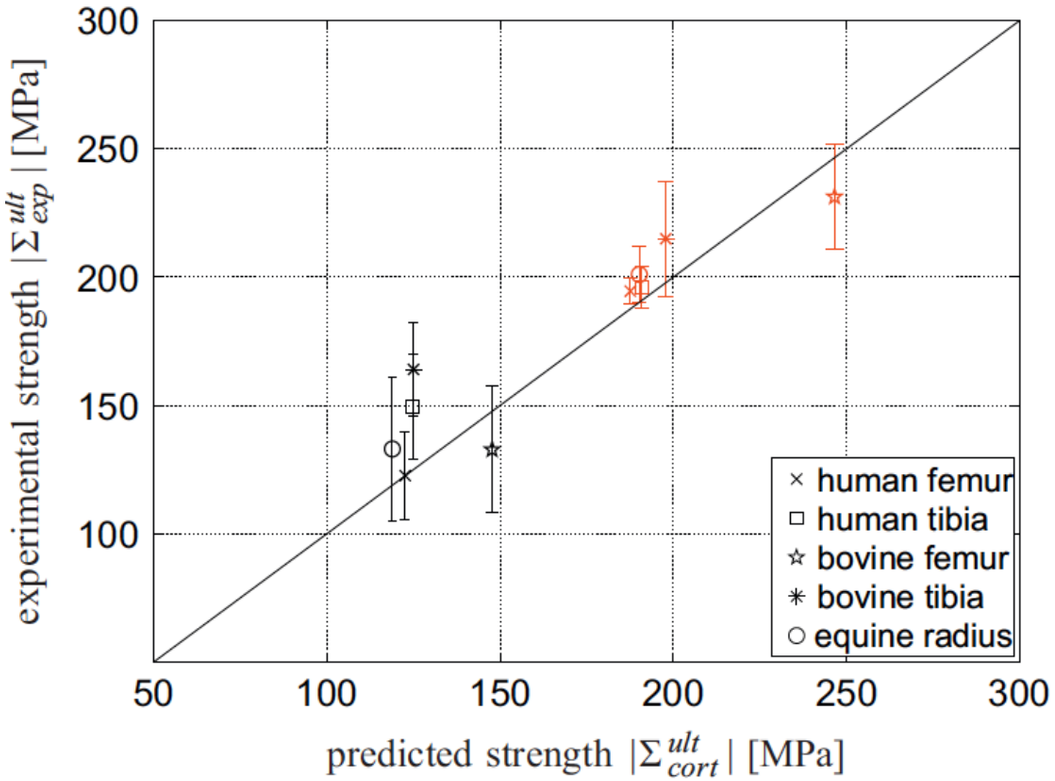
Bone strength:

through definition of failure criteria
for collagen and hydroxyapatite



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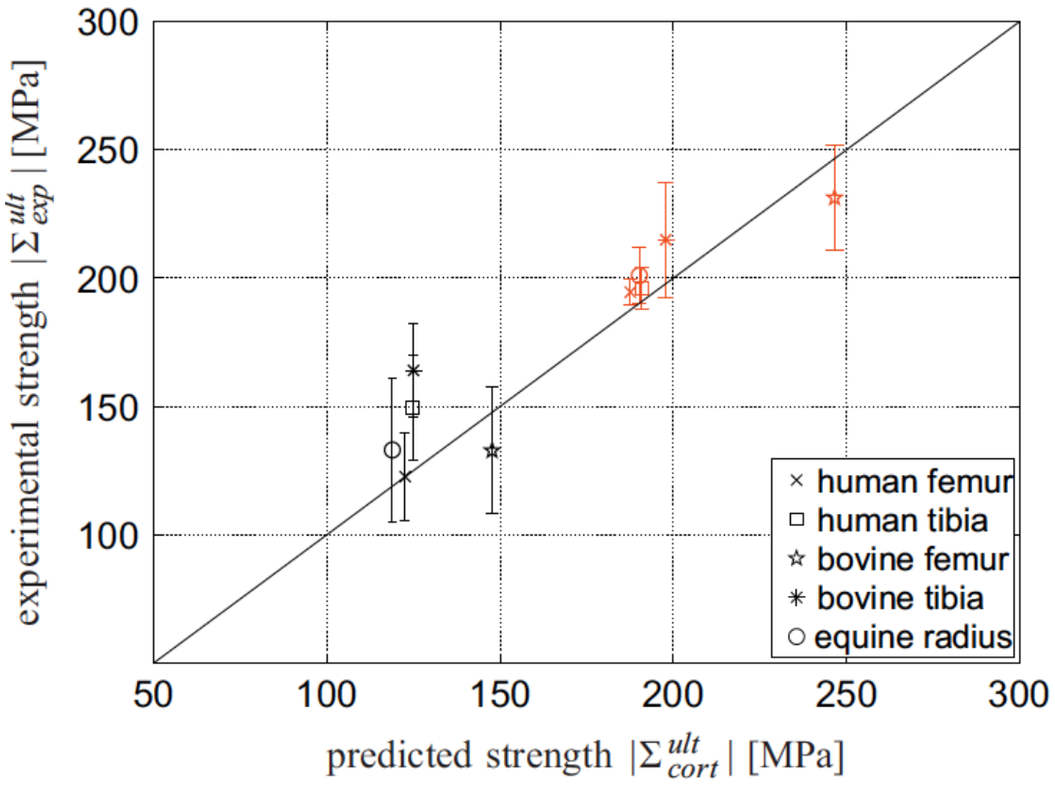

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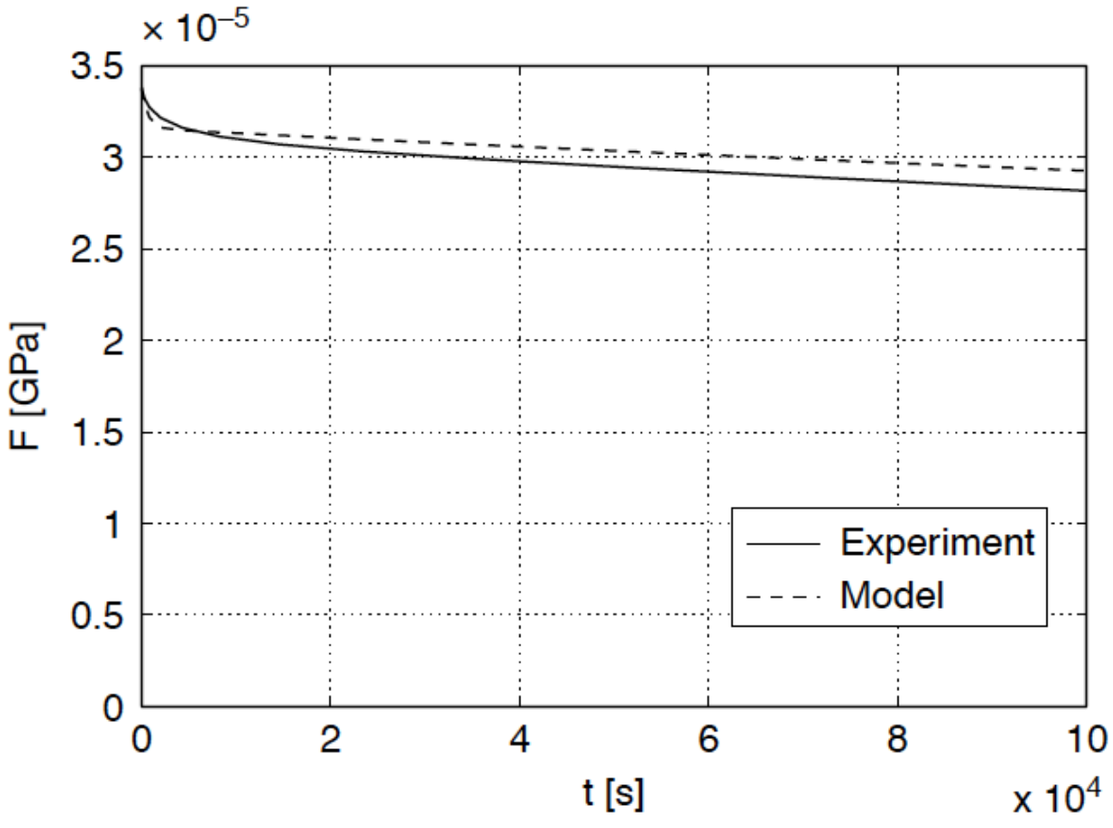
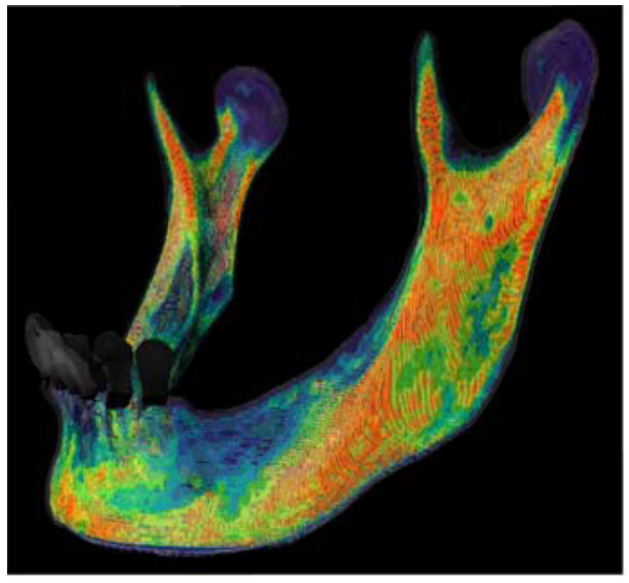
Bone viscoelasticity:
through definition of viscoelastic behavior of hydroxyapatite



Eberhardsteiner et al. (2014), *Computer Methods in Biomechanics and Biomedical Engineering* 17: 48-63

Simulation of Bone Structures

Elastic deformations of human mandible:



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CT image = spatial distribution of voxel-specific grey levels (proportional to attenuation behavior)

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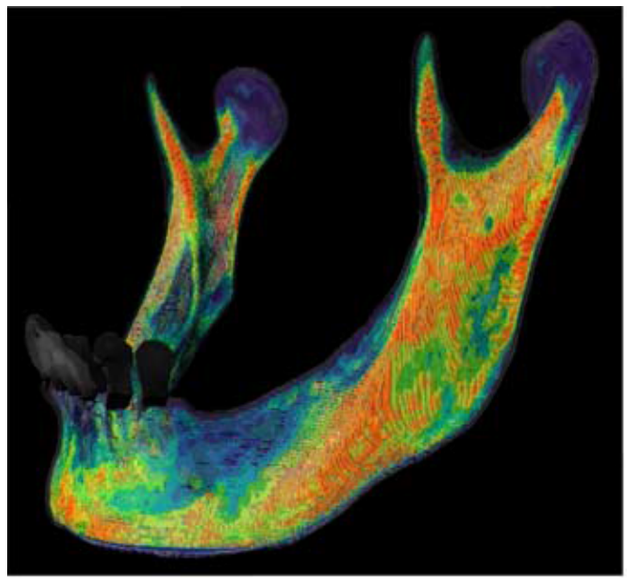

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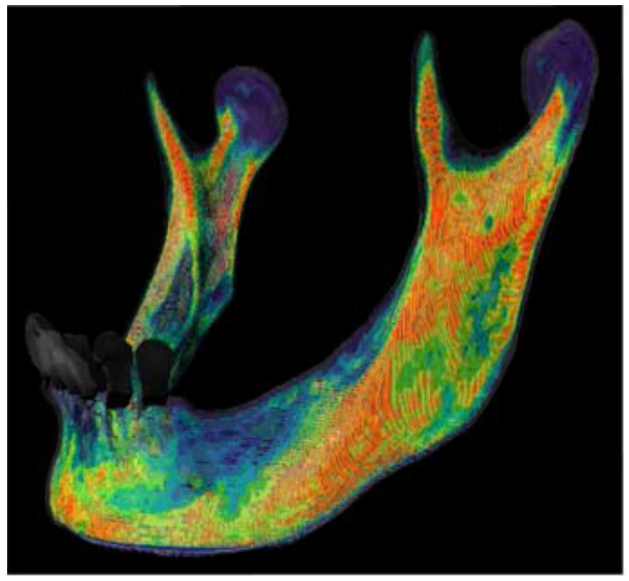

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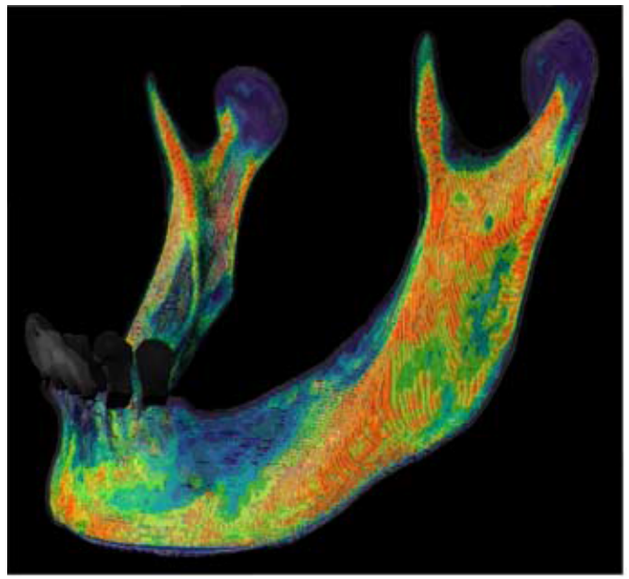

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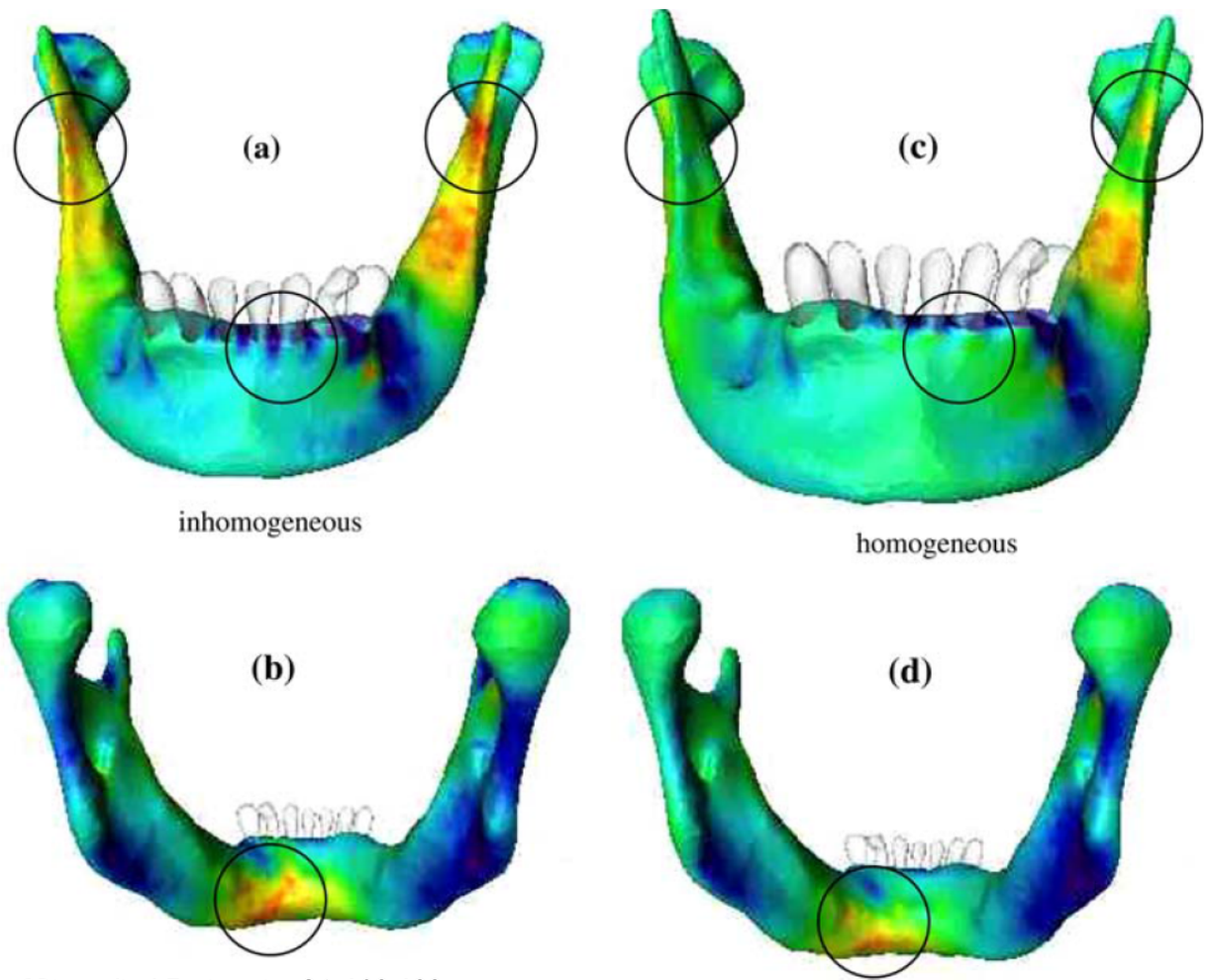
Structural simulations reveal that prescribing more realistic bone stiffness leads to **substantially changed strain and stress distributions**



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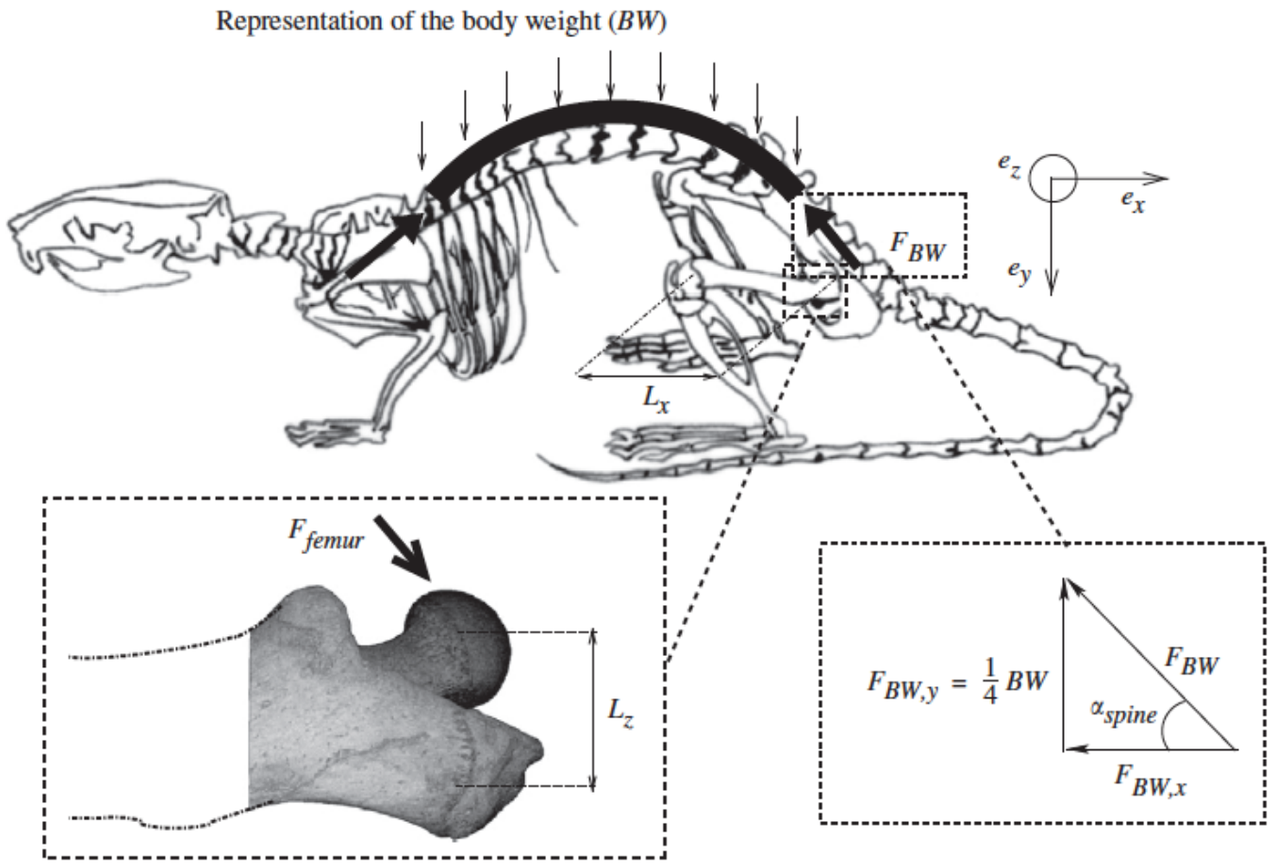
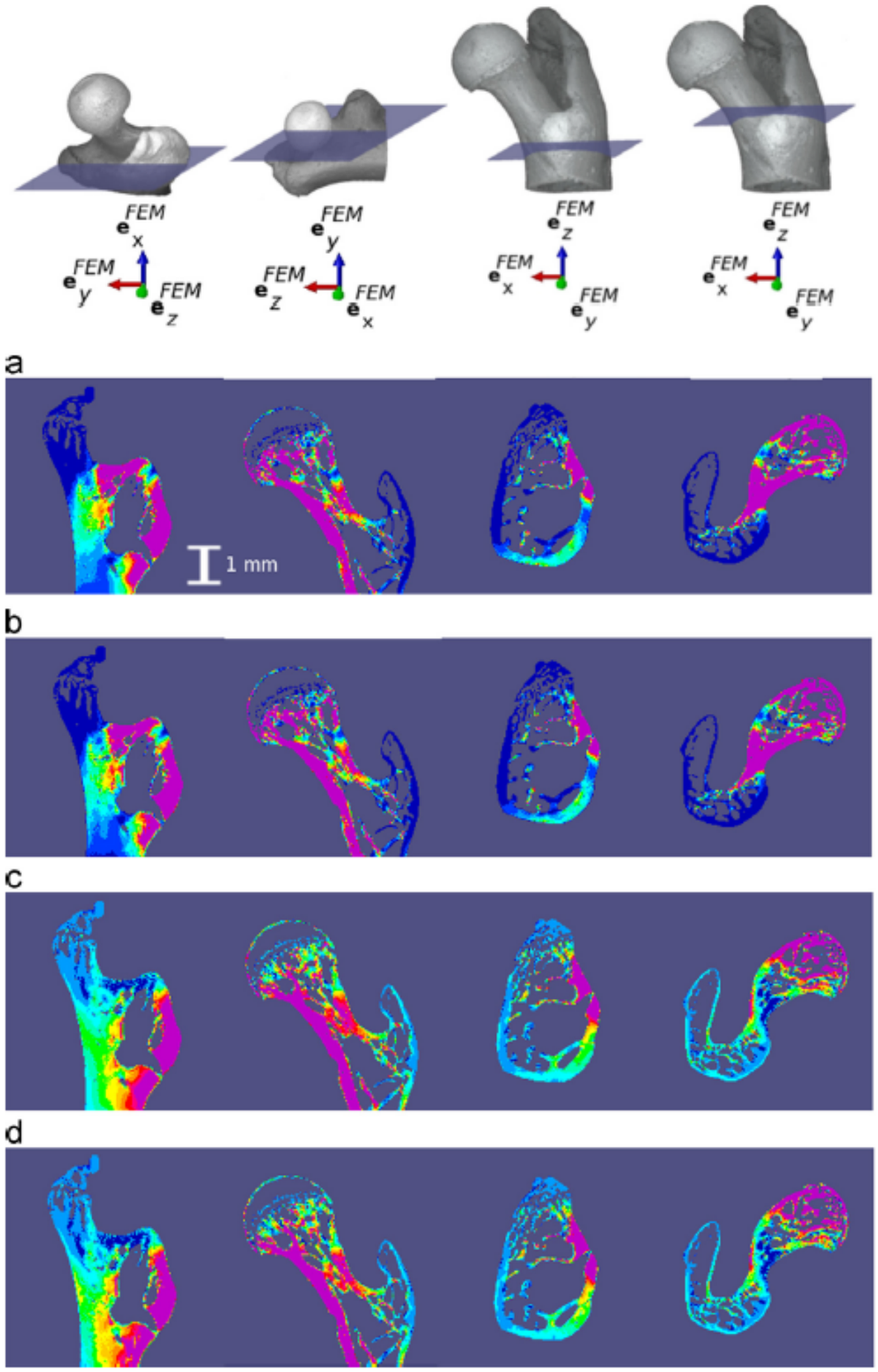
Simulation of Bone Structures

Elastic deformations of mouse femur:



- bone composition considered based on CT data-to-volume fractions conversion technique
- micromechanics provides then map of bone stiffness distribution
- the **effects of various (physiological) load cases can be easily studied**



Blanchard et al. (2013), *Journal of* Biomechanics 46: 2710-2721

Stiffness and Strength of Biomaterials

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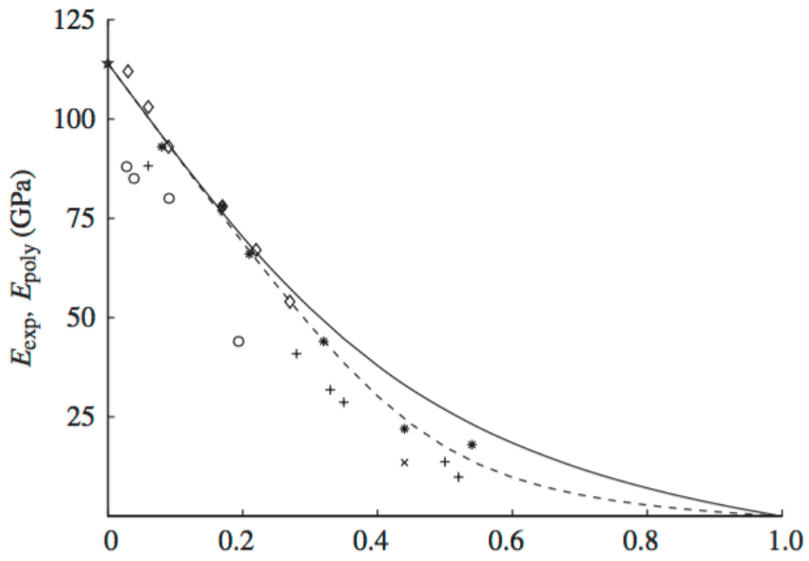
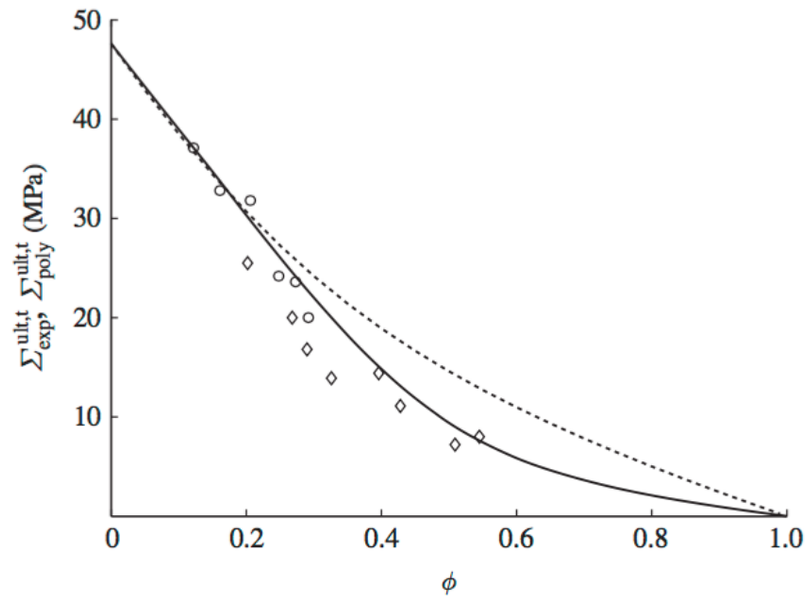
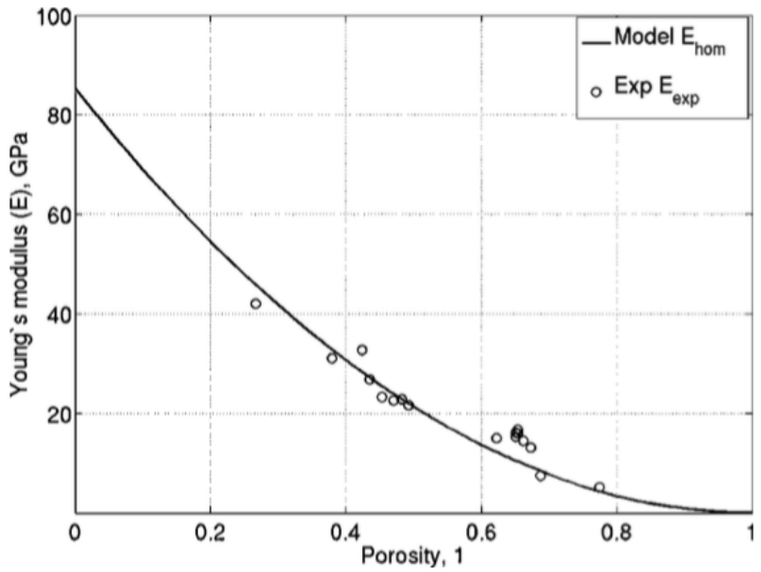
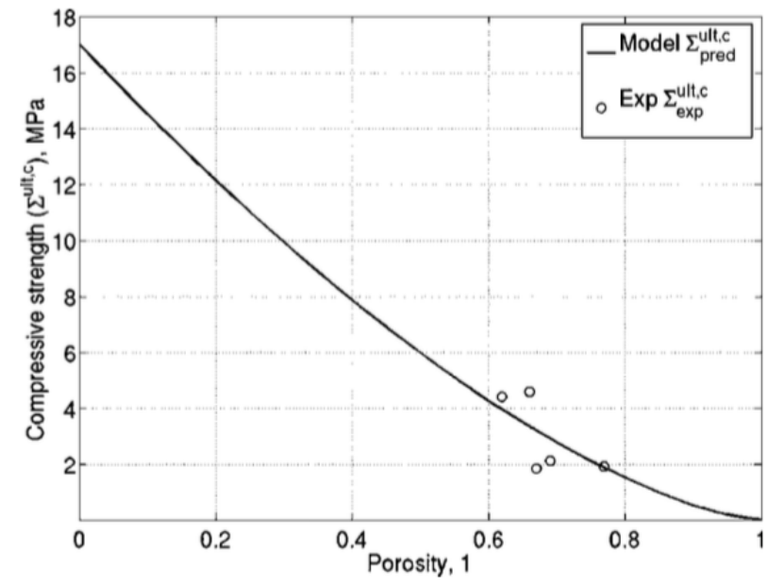
Fritsch et al. (2010), *Philosophical Transactions A* 80: 020905



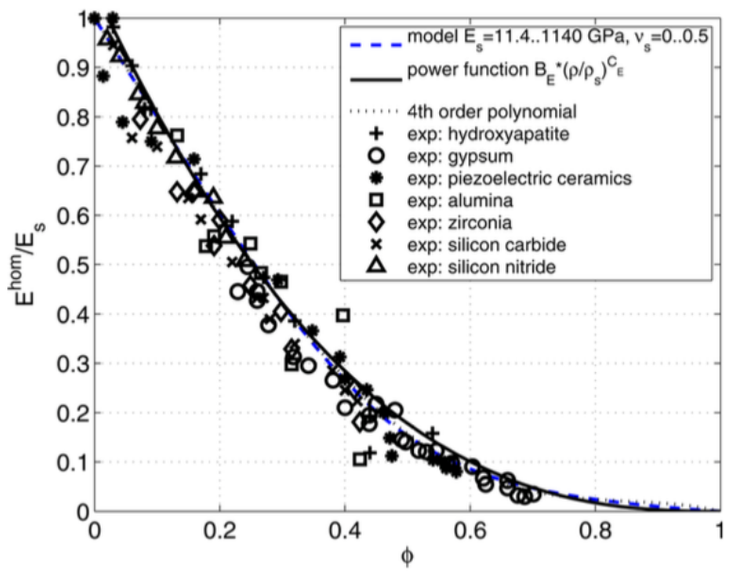


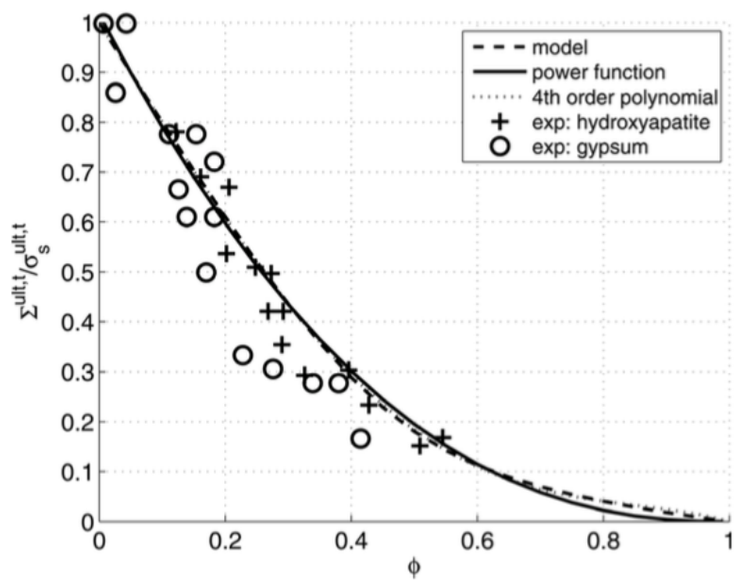
Malasoma et al. (2008), *Advances in Applied Ceramics* 107: 277-286





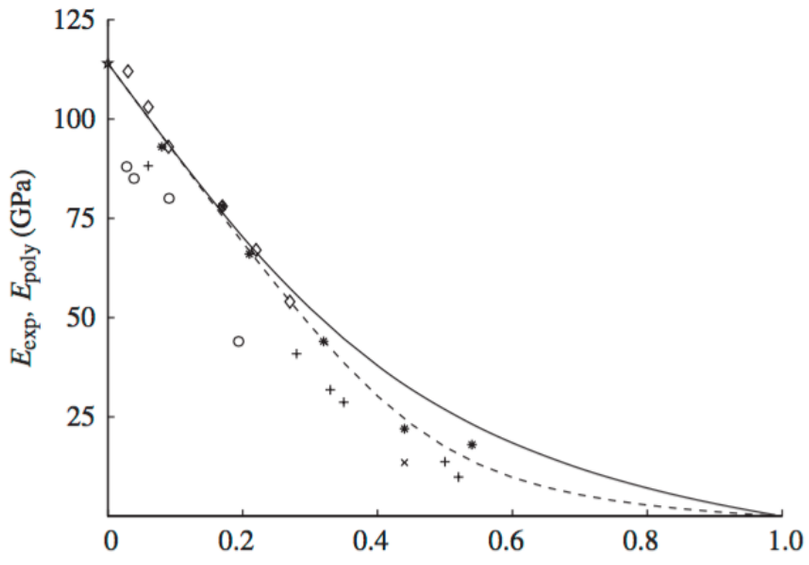
Fritsch et al. (2013), *Journal of Applied Mechanics* 80: 020905

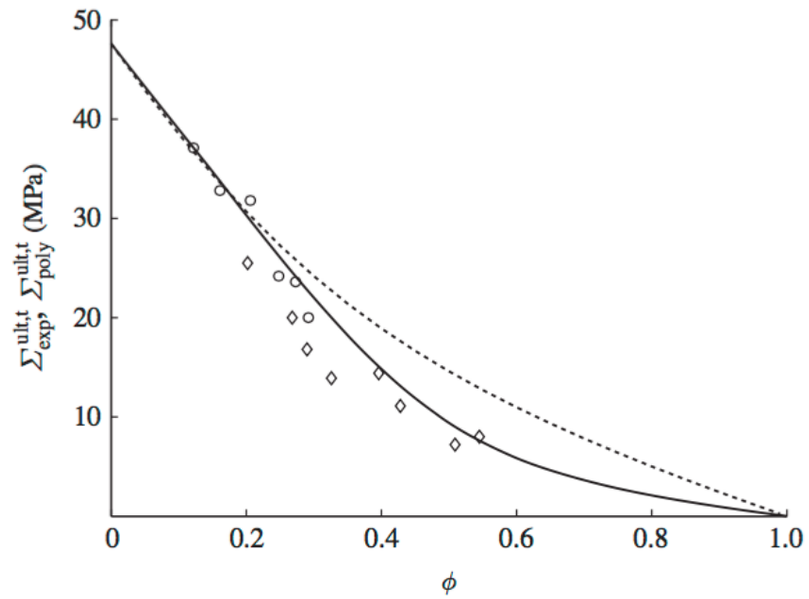




Stiffness and Strength of Biomaterials

Fritsch et al. (2010), *Philosophical Transactions A* 80: 020905





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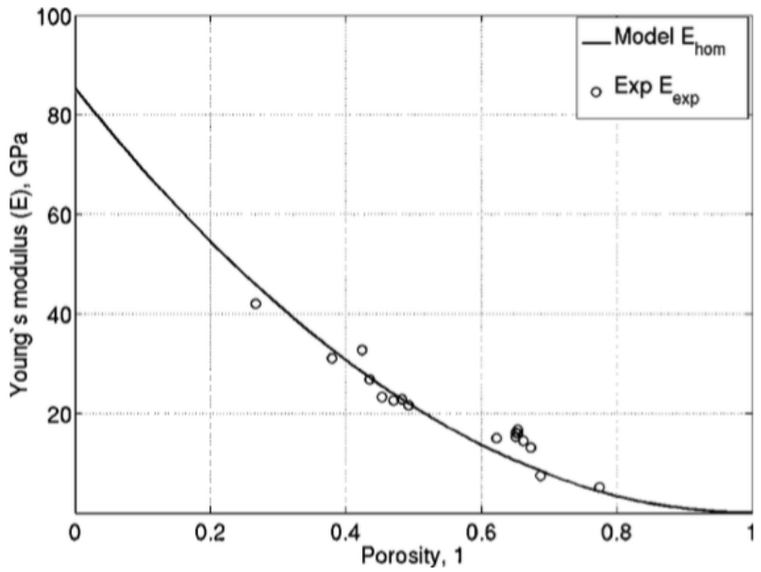

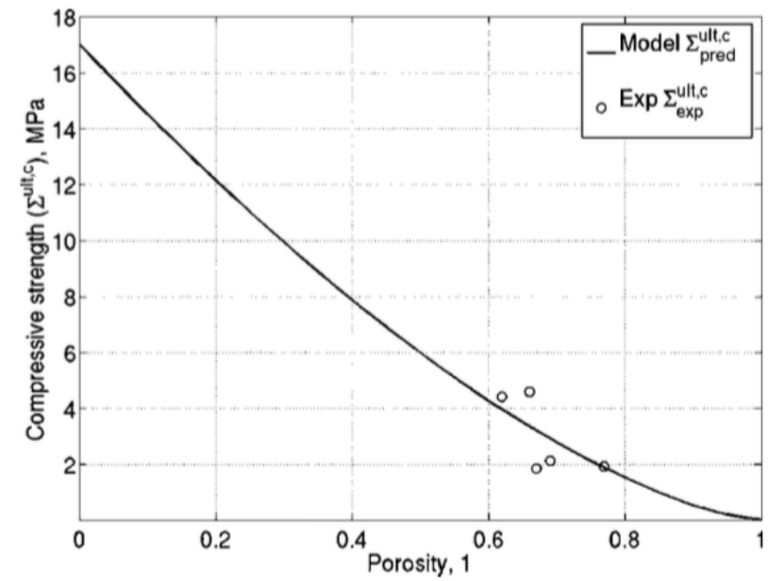

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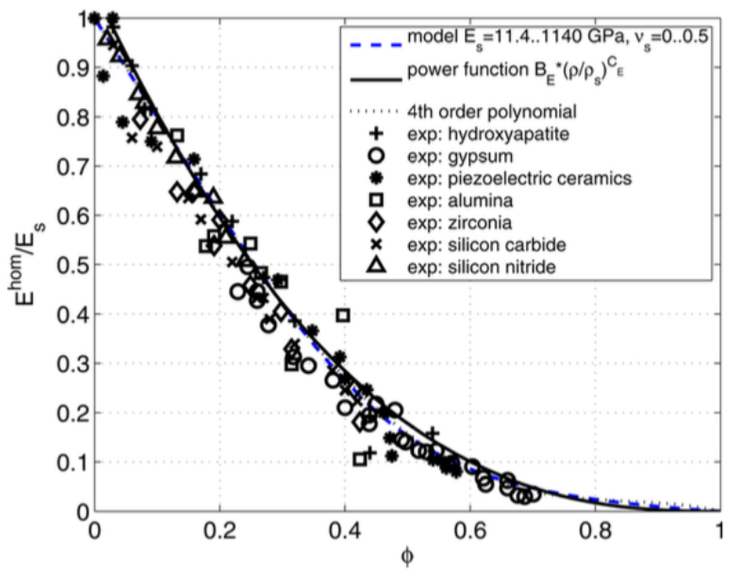

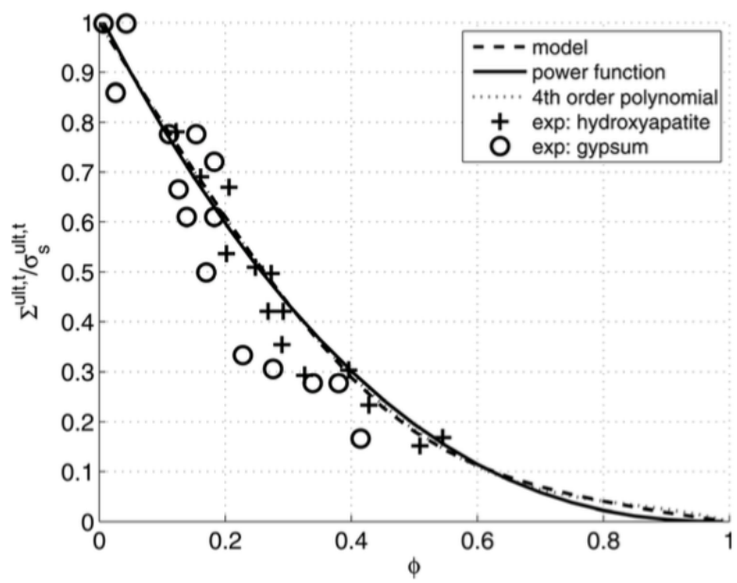

➡ **good agreement** between model predictions and experimental data

Stiffness and Strength of Biomaterials

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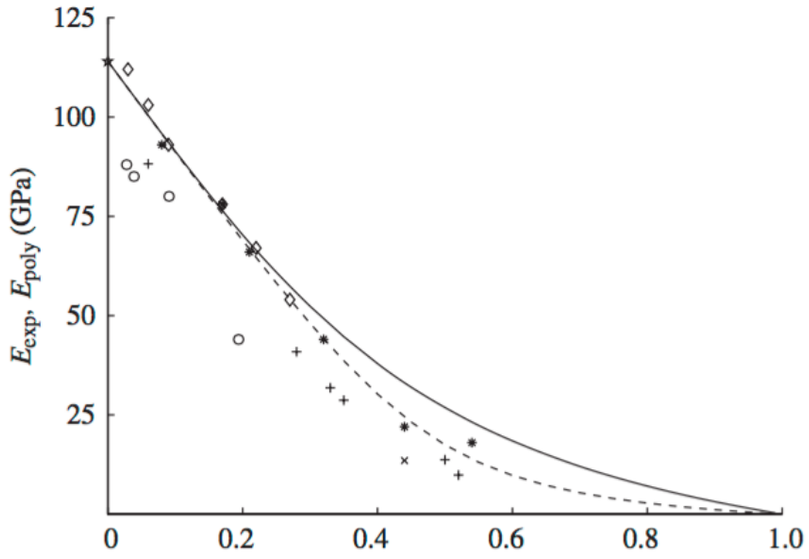

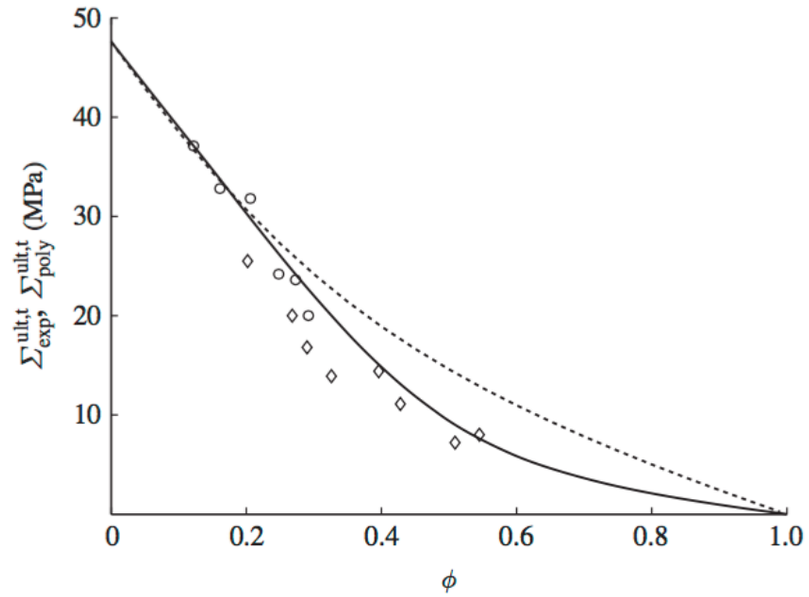

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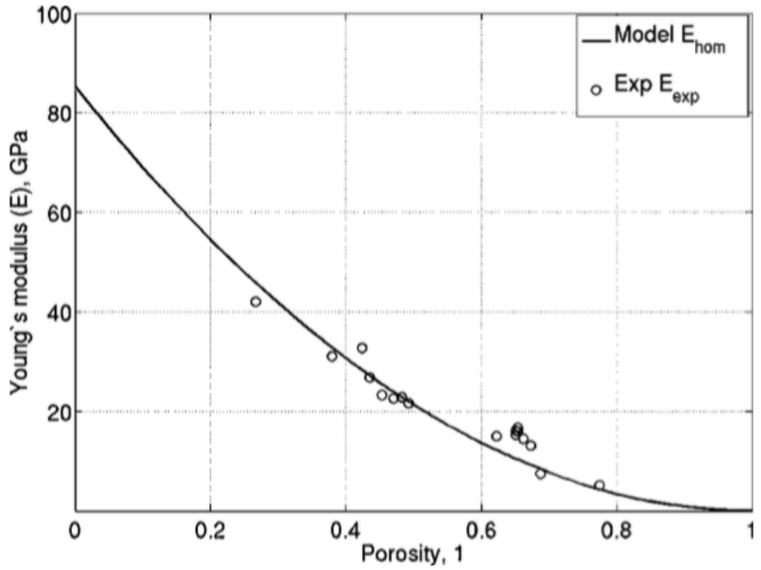

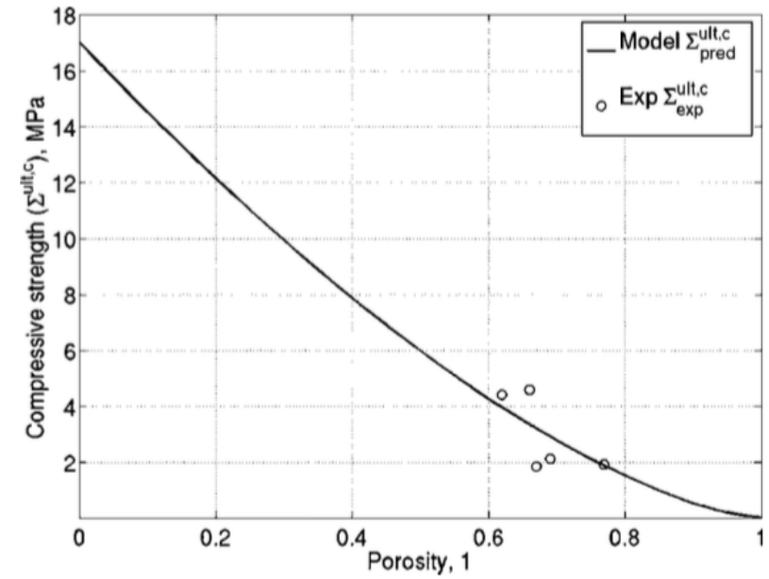

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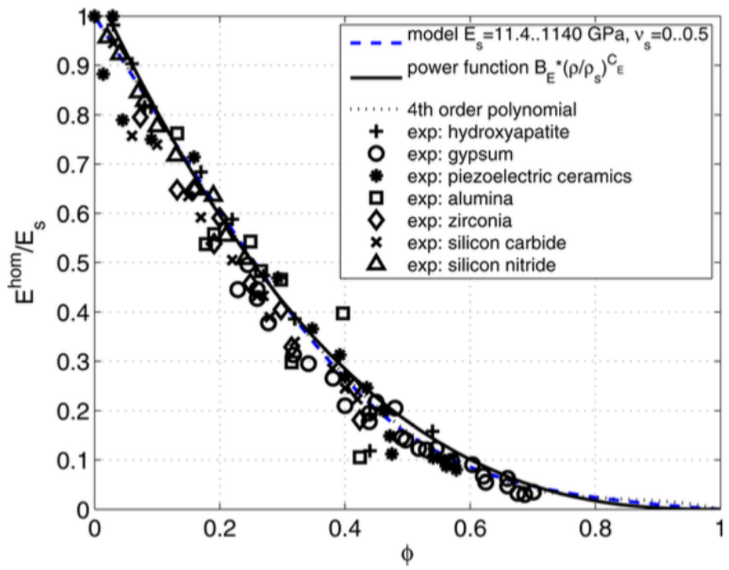

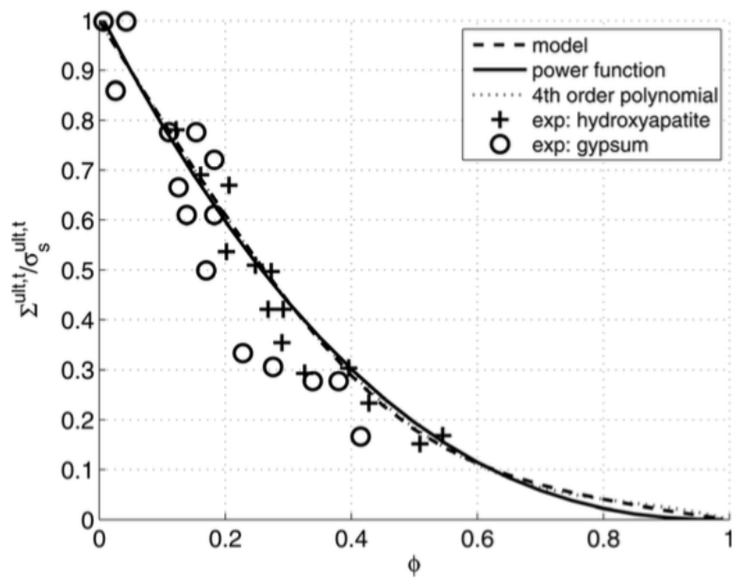

- ➡ **good agreement** between model predictions and experimental data
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Stiffness and Strength of Biomaterials

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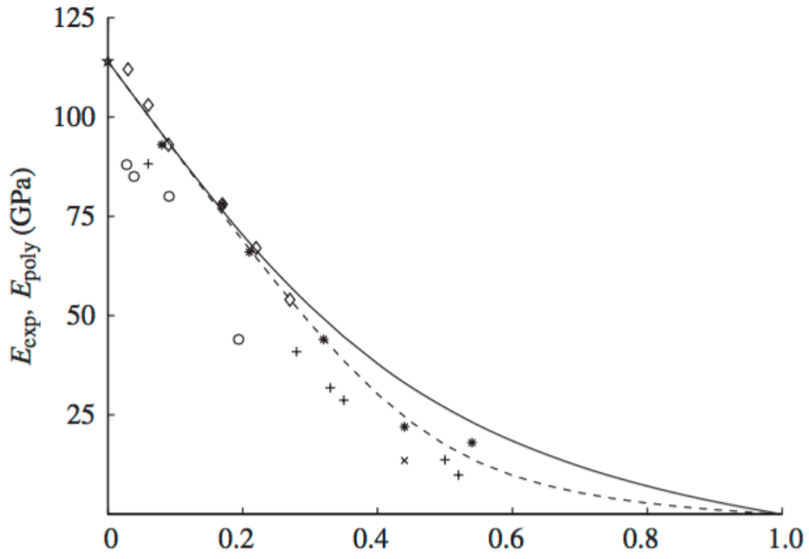

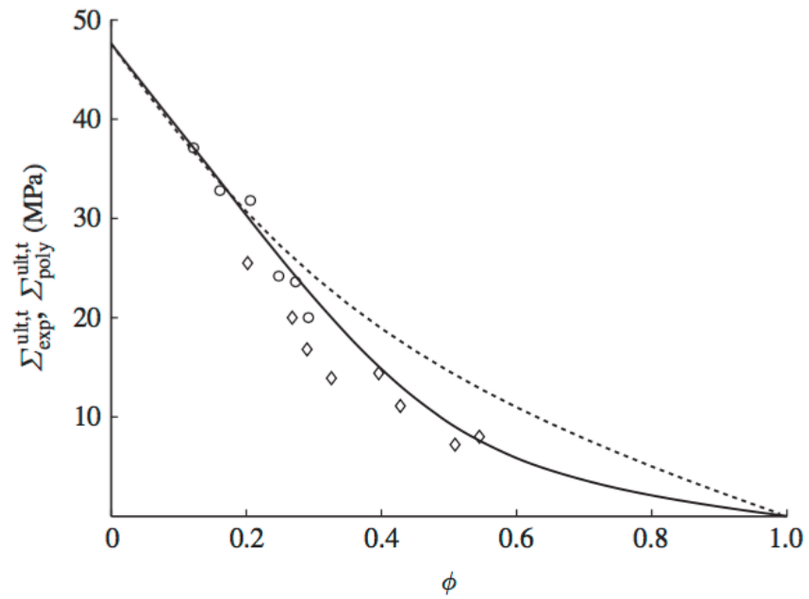

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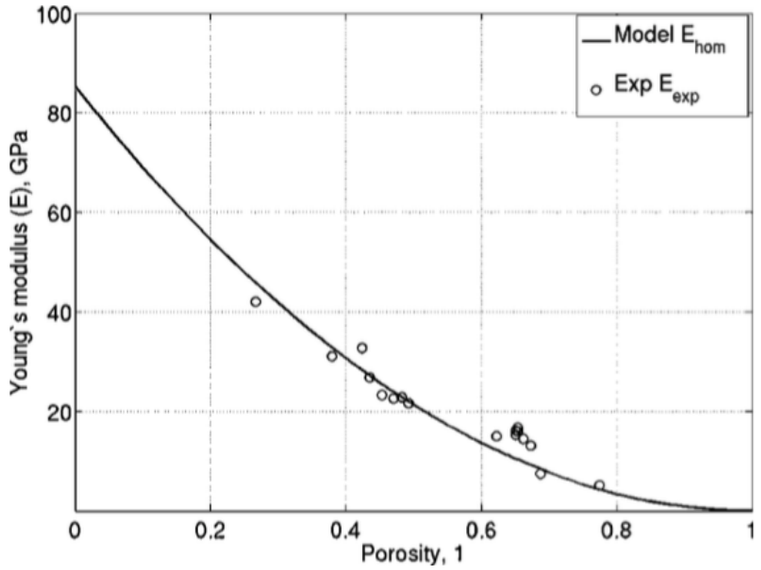

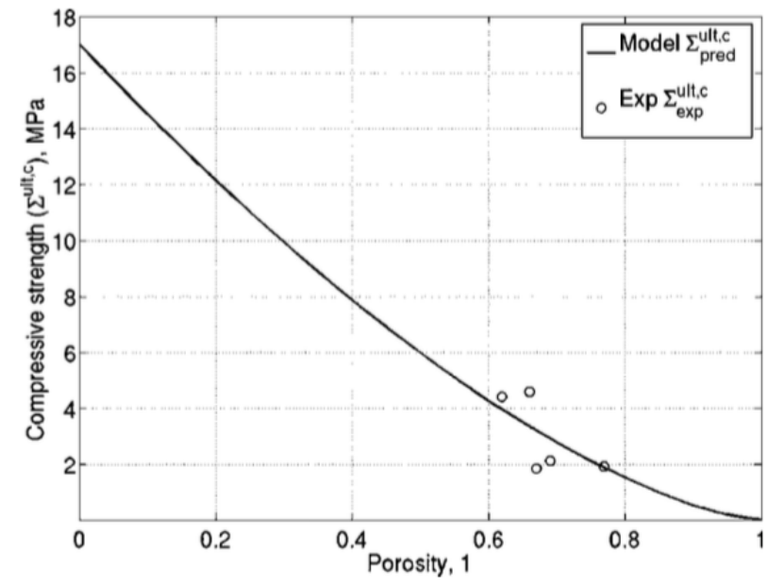

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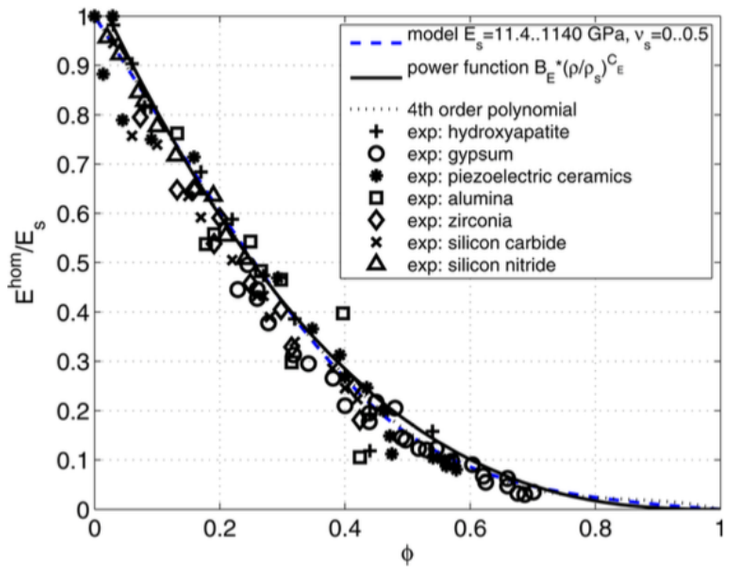

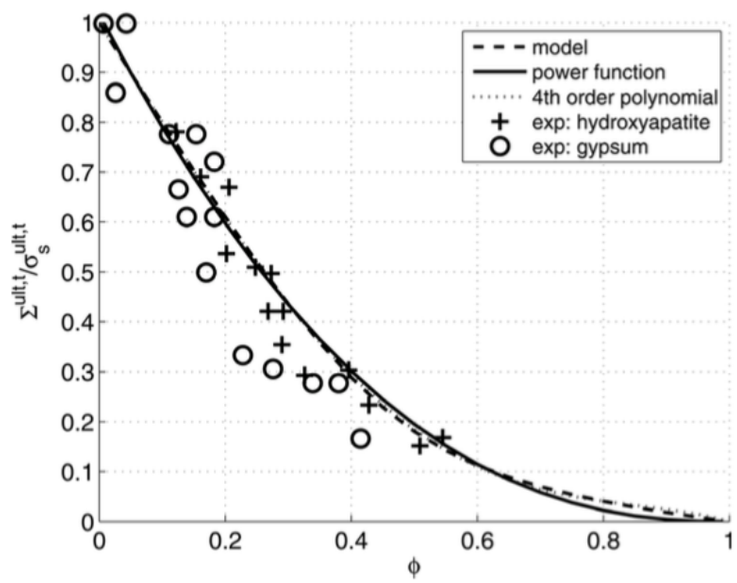

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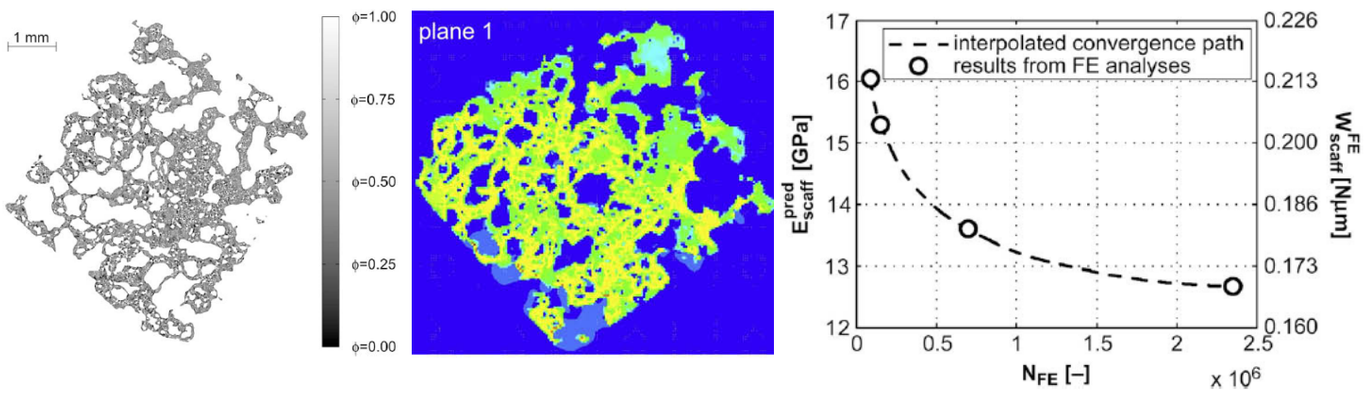
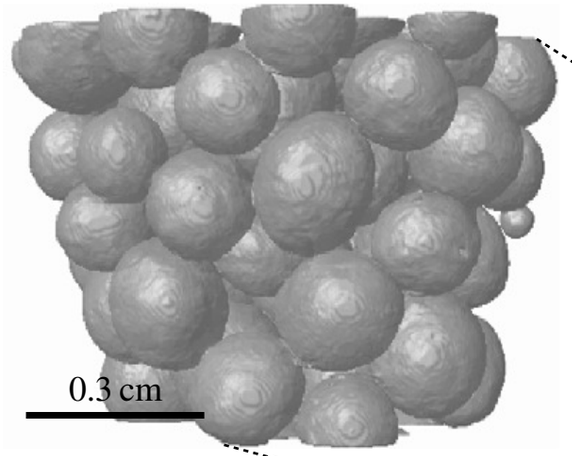


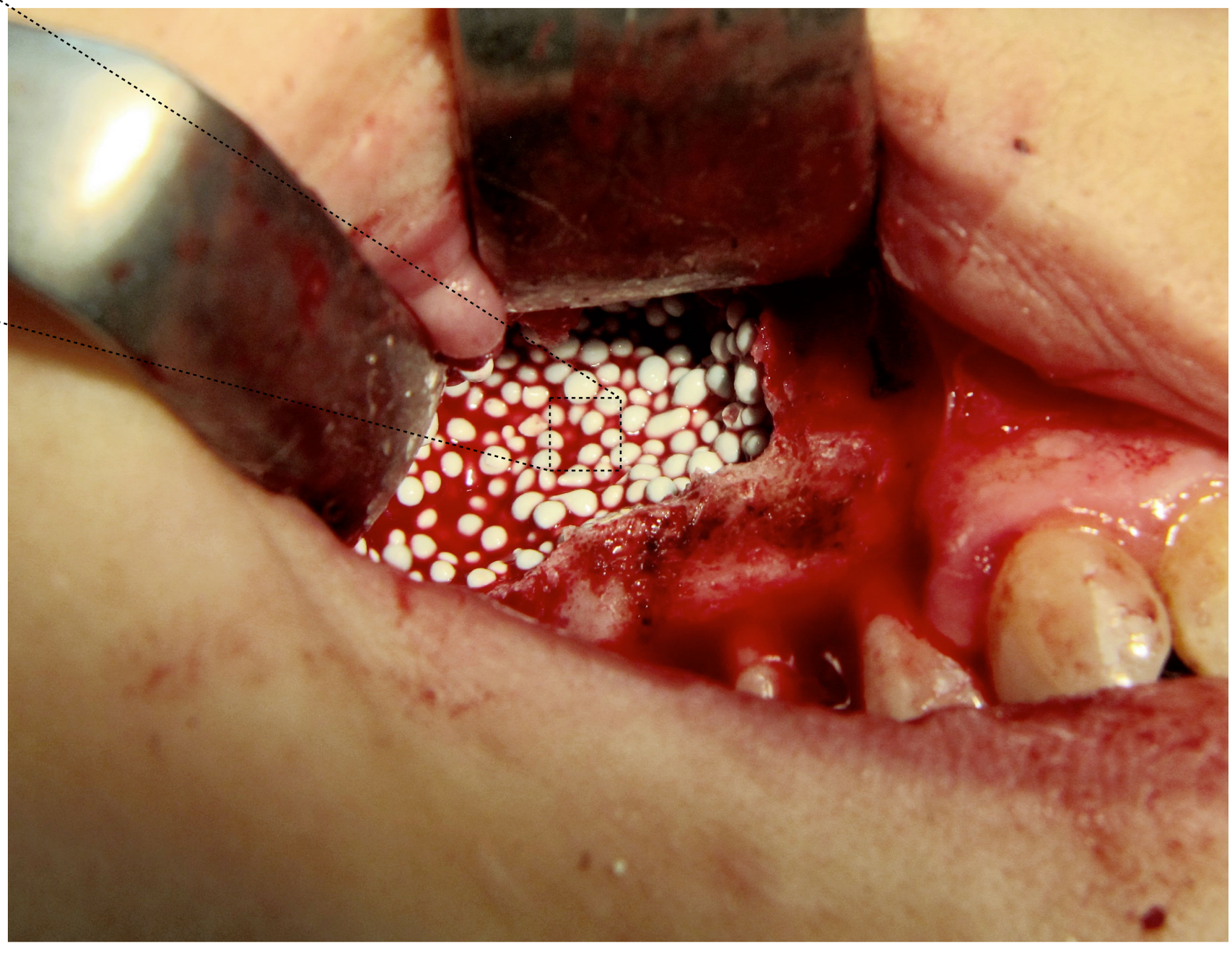
Scheiner et al. (2009), *Biomaterials* 30: 2411-2419

Consideration of Bone Regeneration

Consideration of Bone Regeneration

Definition of the Studied Material





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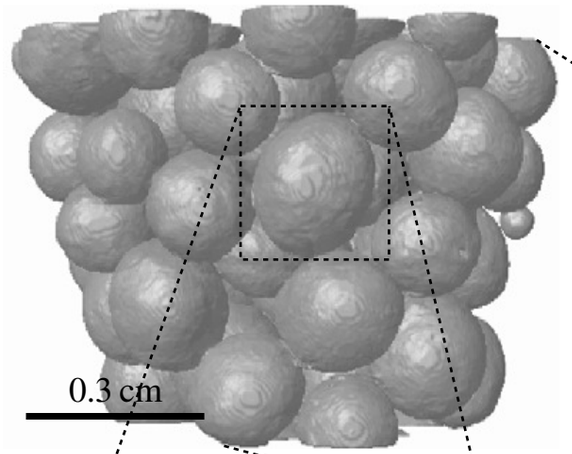

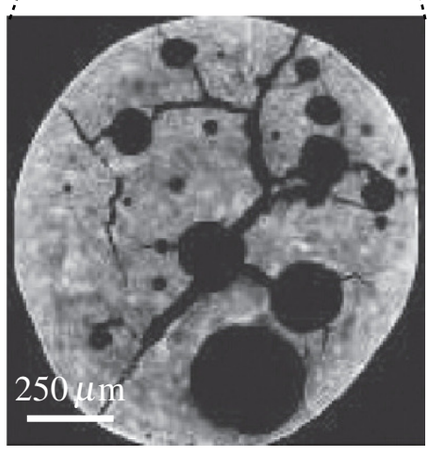

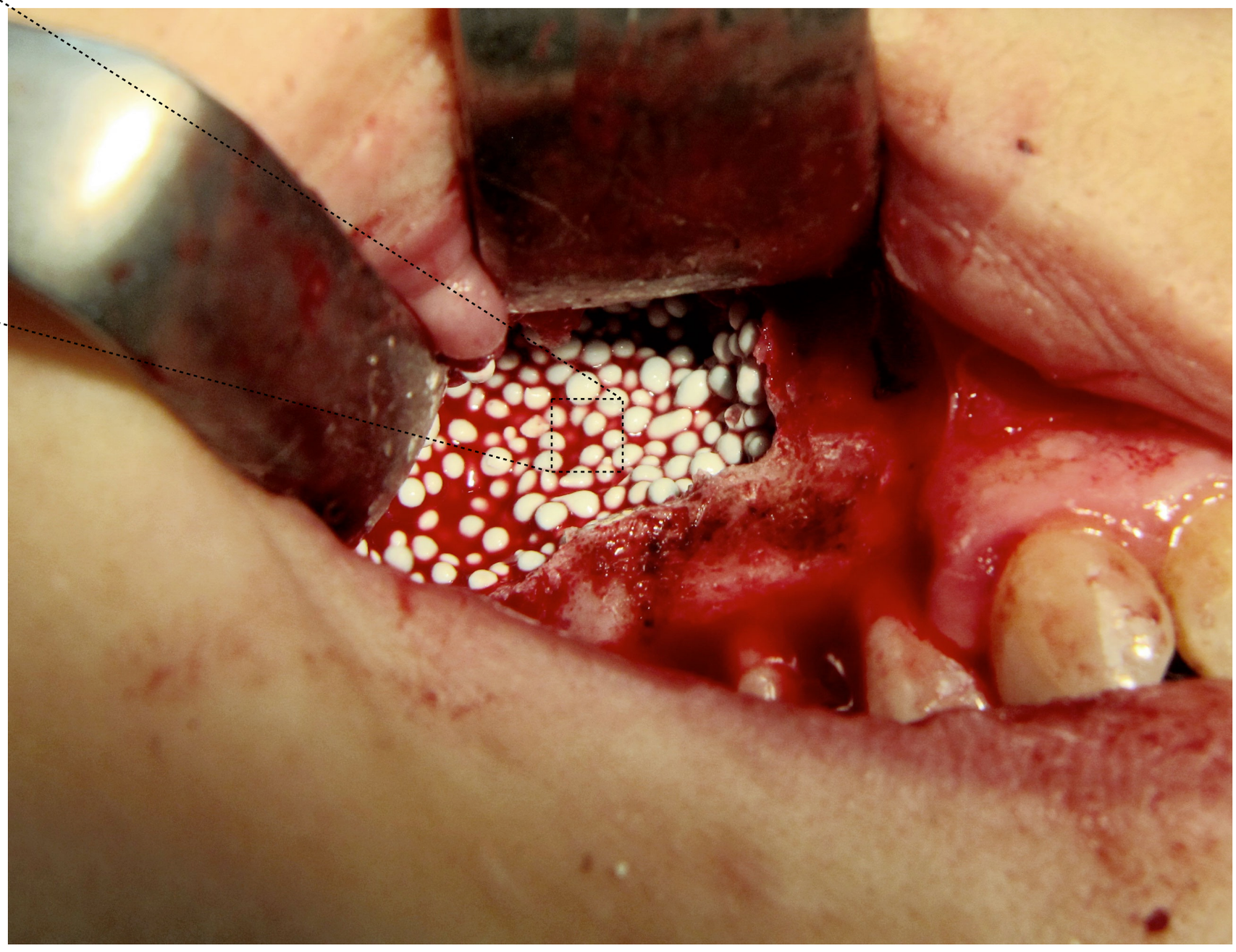

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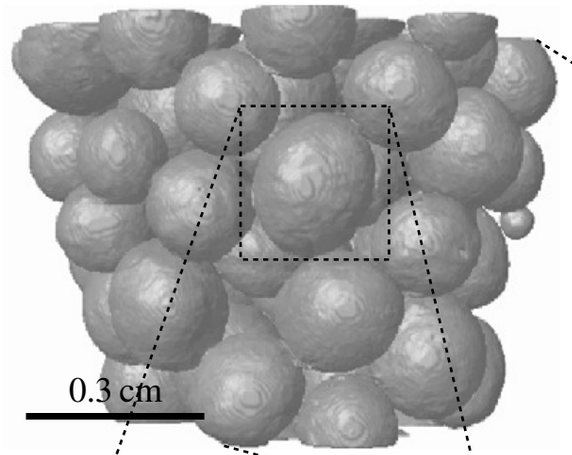
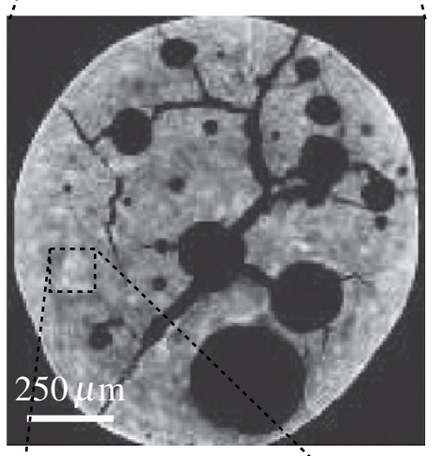
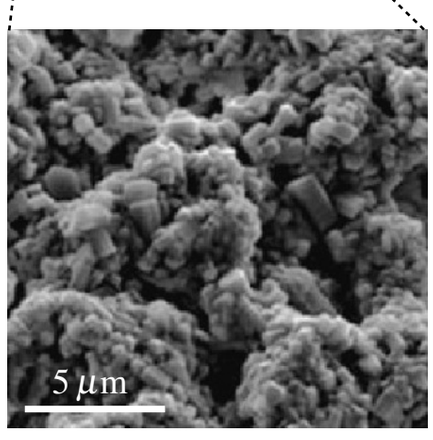
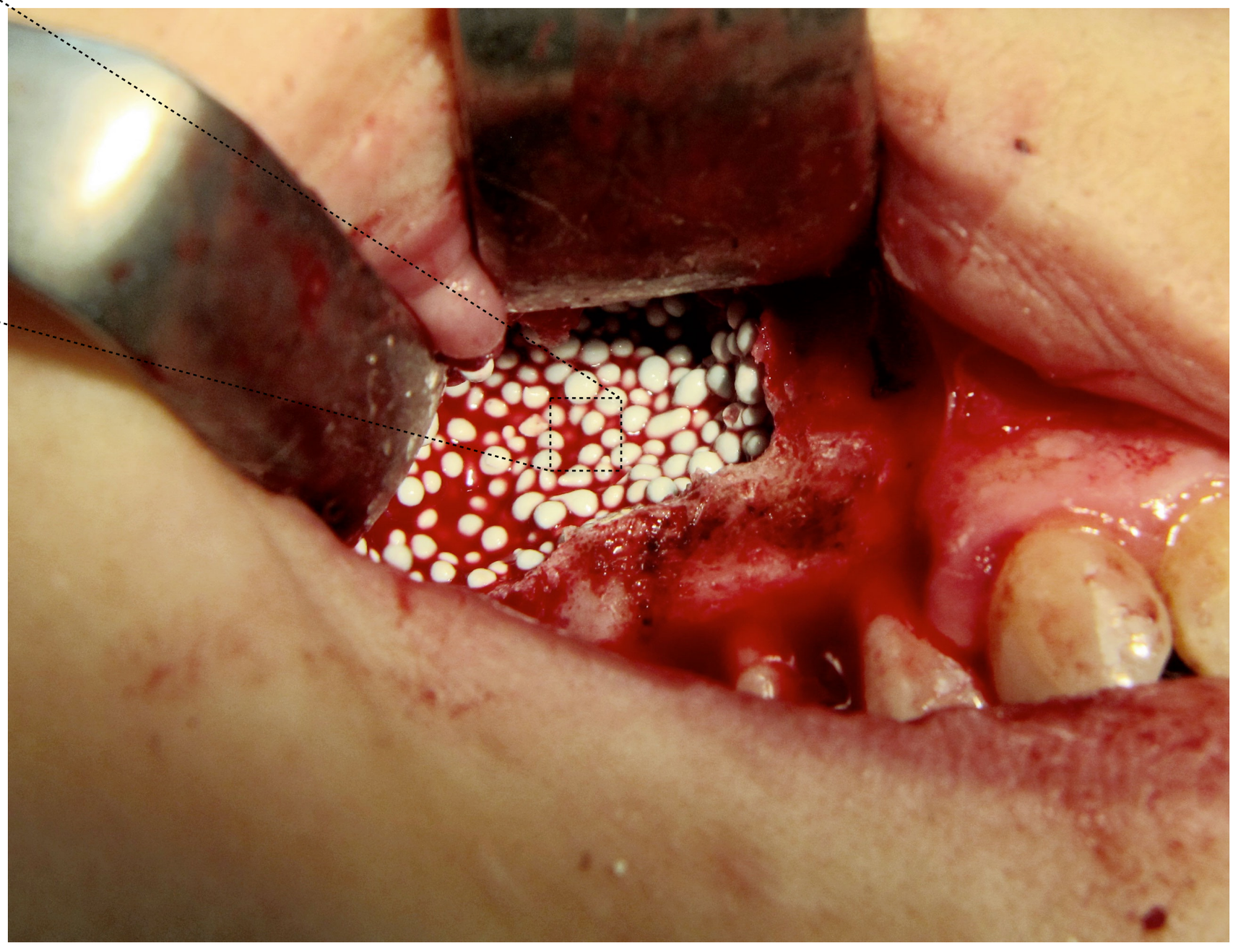






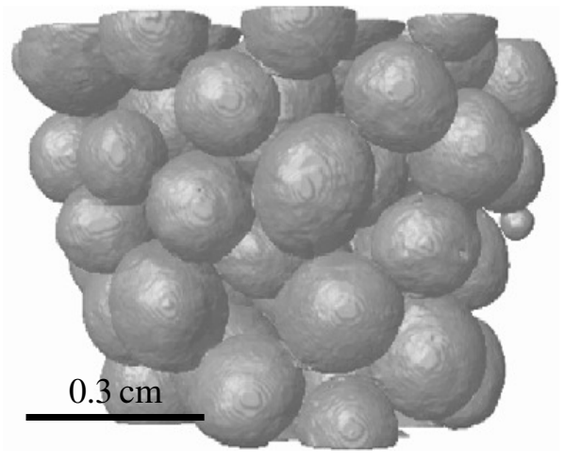


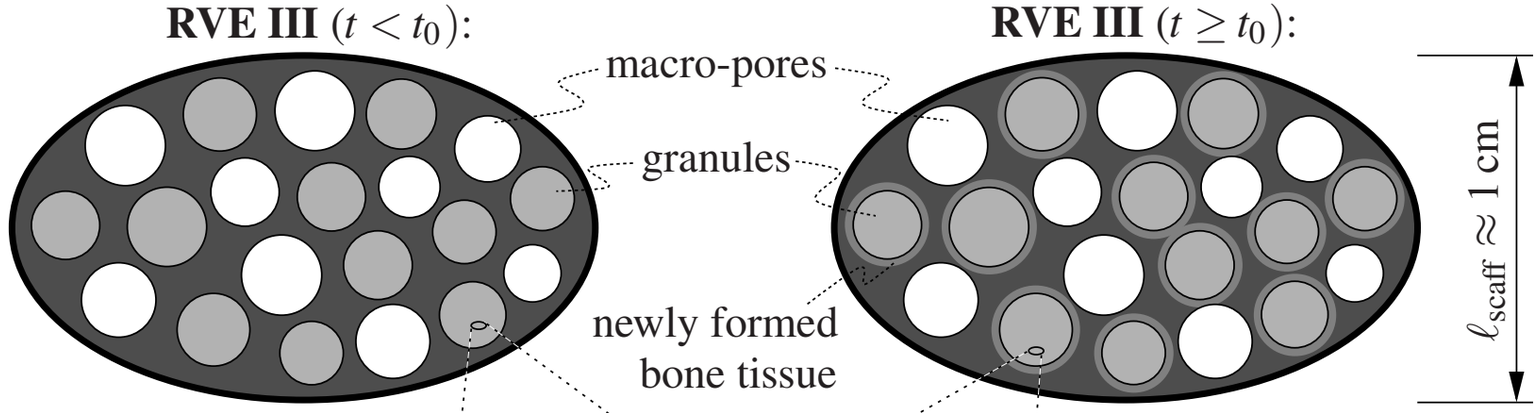
Definition of the Studied Material

Images on distinct scales

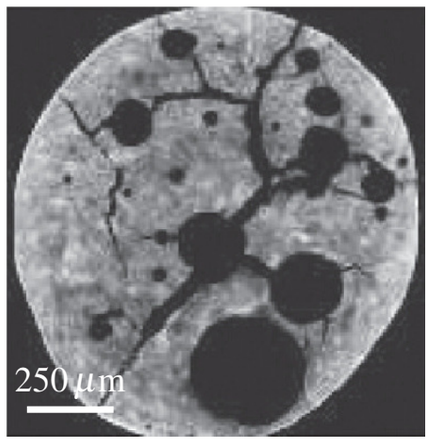
Micromechanical representation

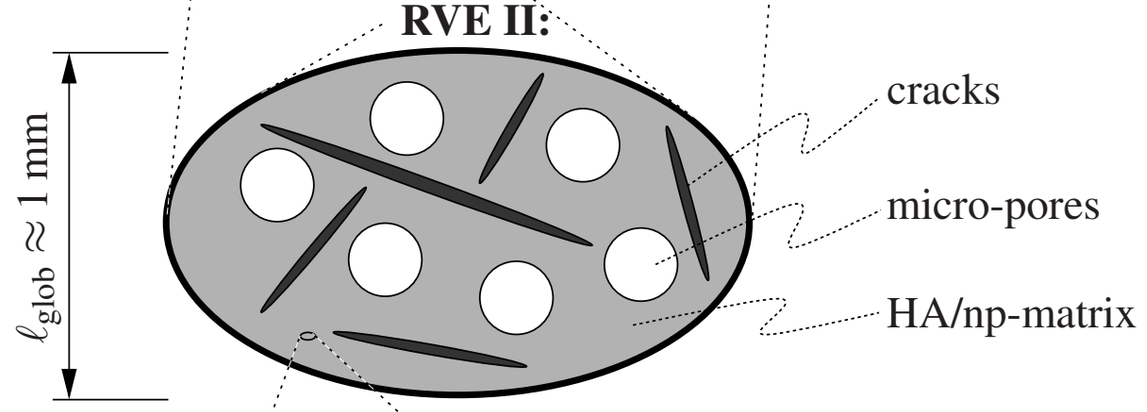
Hierarchical level III: macro-porous scaffold material, subjected to bone regeneration



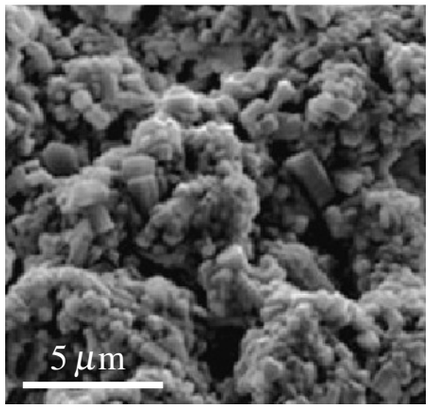


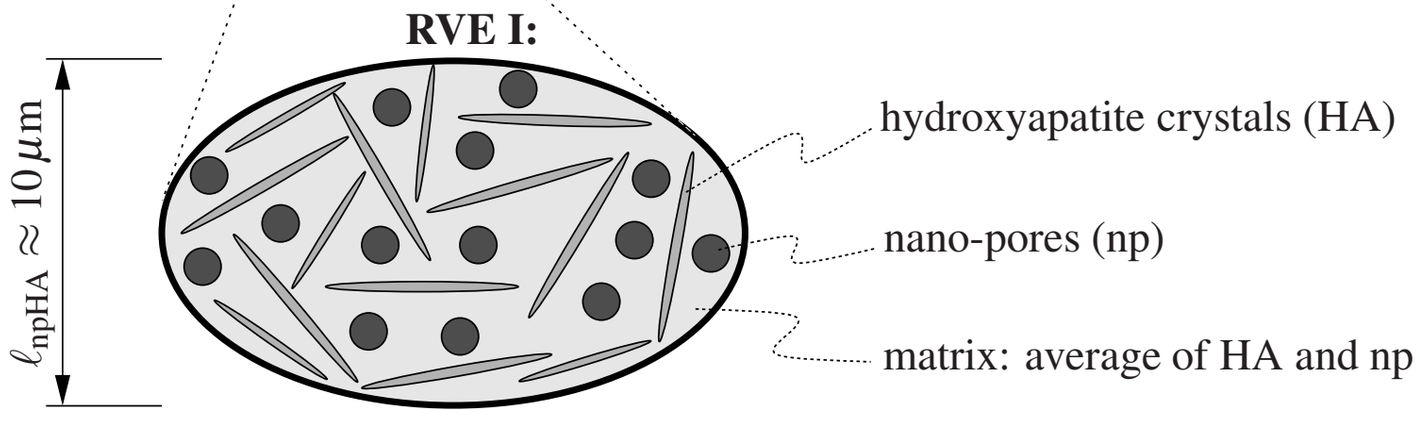
Hierarchical level II: pre-cracked, micro-porous globule matrix





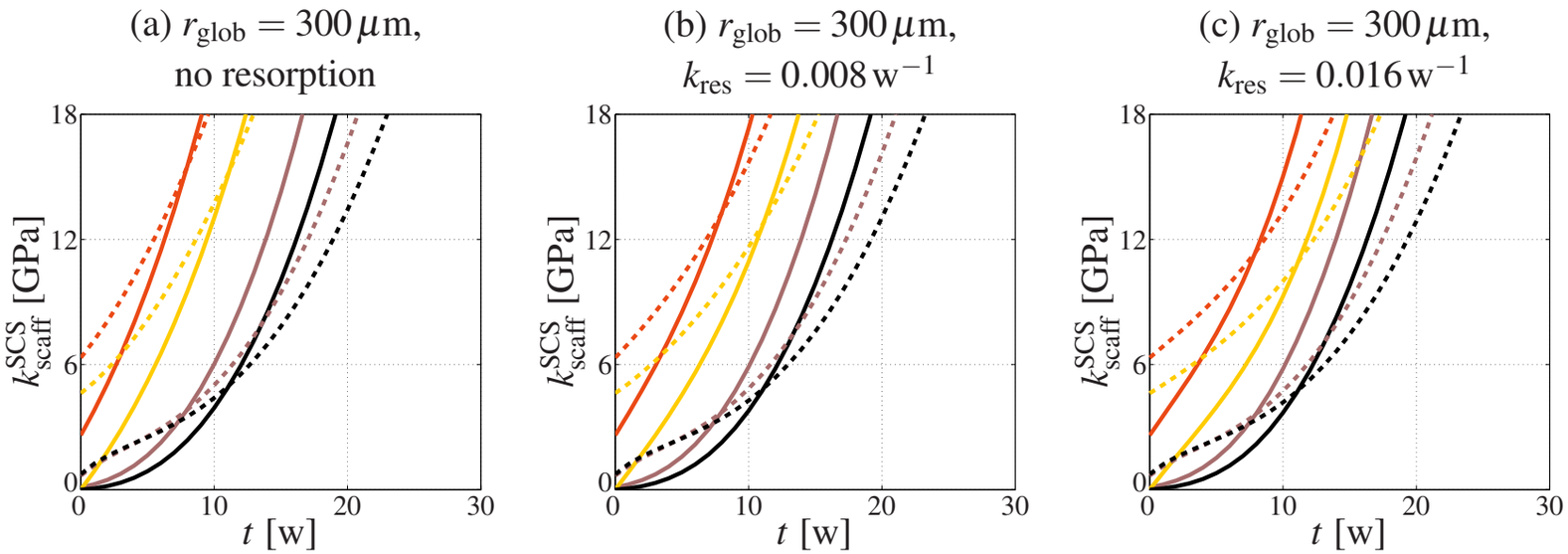
Hierarchical level I: nano-porous hydroxyapatite polycrystal





Scheiner et al., manuscript in preparation

Homogenized Bulk Modulus of Scaffold



Simulations with:

- varying globule radii
- varying resorption rate

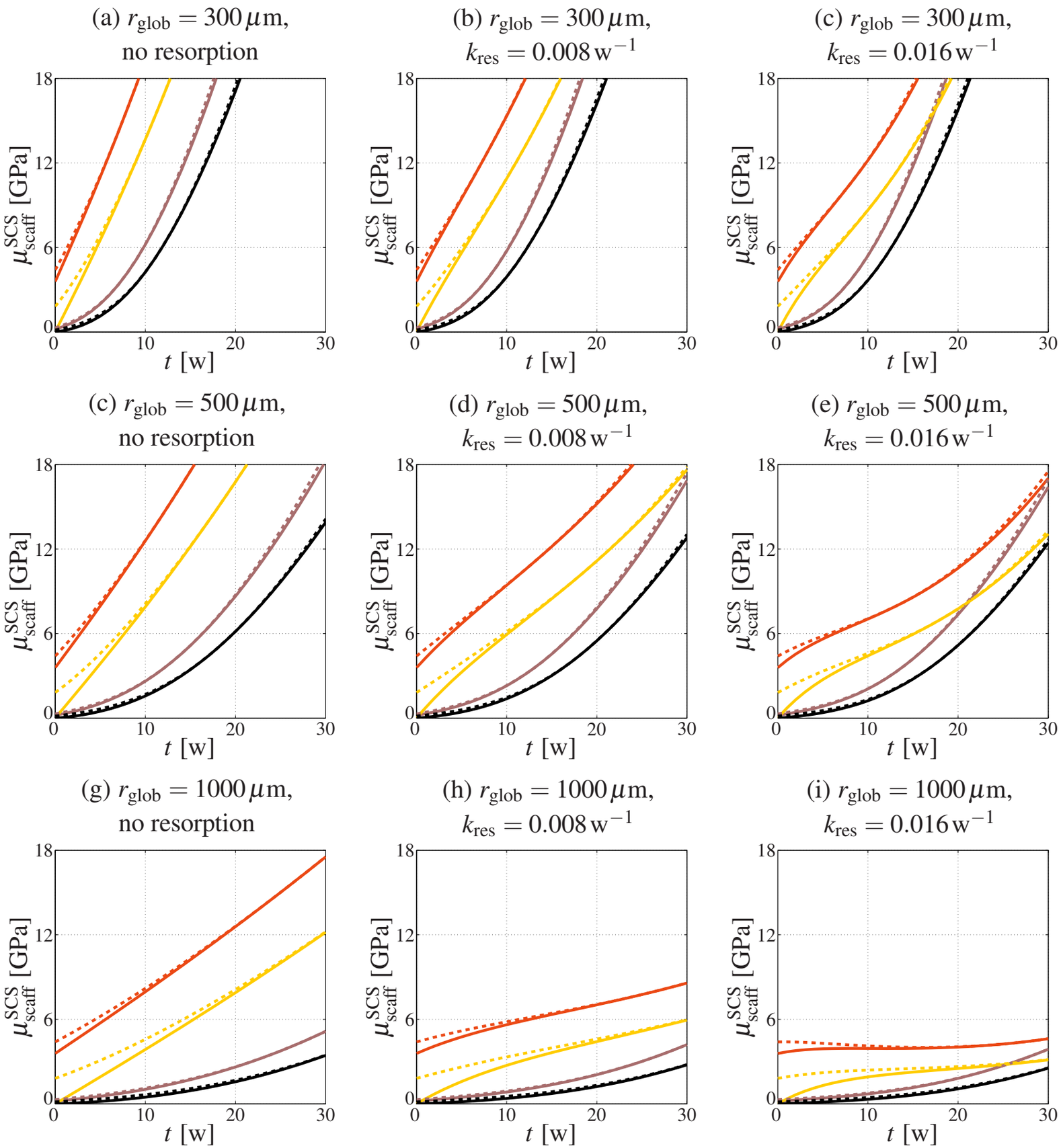
Figure legend:

- —— / - - - $f_{map} = 0.4,\ \varepsilon = 0$
- —— / - - - $f_{map} = 0.4,\ \varepsilon = 10$
- —— / - - - $f_{map} = 0.5,\ \varepsilon = 0$
- —— / - - - $f_{map} = 0.5,\ \varepsilon = 10$

drained / undrained macropores

Scheiner et al., manuscript in preparation

Homogenized Shear Modulus of Scaffold



Simulations with:

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drained / undrained macropores

Scheiner et al., manuscript in preparation

Time for a Short Reflection

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Q1: But what drives the **development of these volume fractions** in physiological conditions?

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A: Cells and other biological factors; they respond to specific biochemical and mechanical stimuli

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Q1: But what drives the **development of these volume fractions** in physiological conditions?

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Q2: Is it possible to **relate the mechanical properties** of bone/biomaterials to the underlying **biological and mechanical boundary conditions**?

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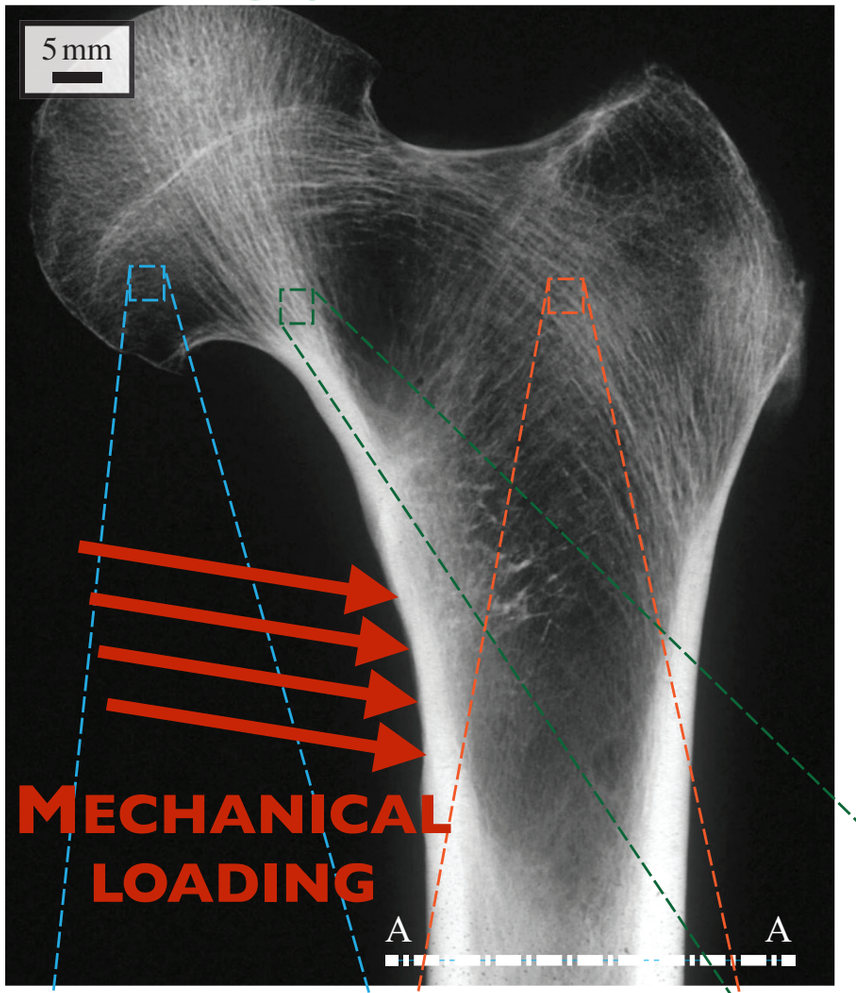
A: Cells and other biological factors; they respond to specific biochemical and mechanical stimuli

Q2: Is it possible to **relate the mechanical properties** of bone/biomaterials to the underlying **biological and mechanical boundary conditions**?

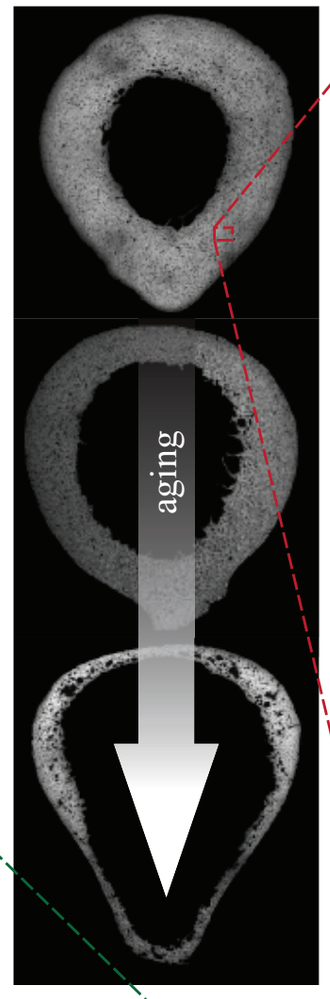
A: **Yes!** By means of adequate **SYSTEMS BIOLOGY MODELS**

BONE REMODELING: PROBLEM DEFINITION

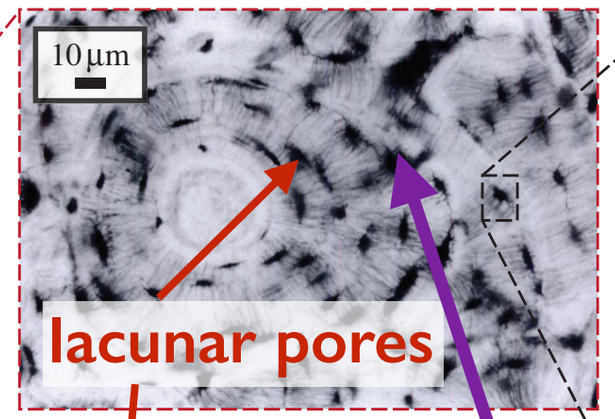
radiograph of human femur[a]



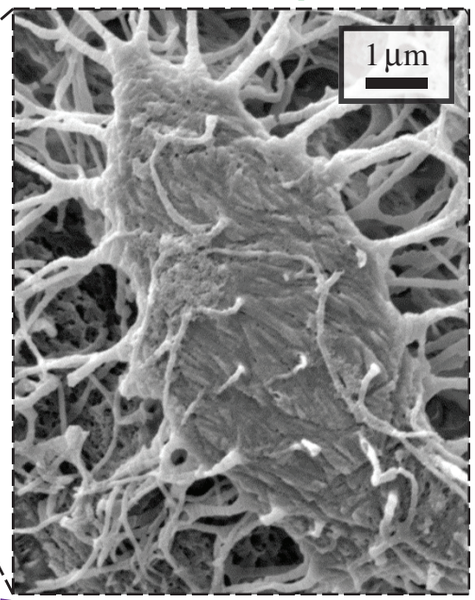
cross section A-A[b]



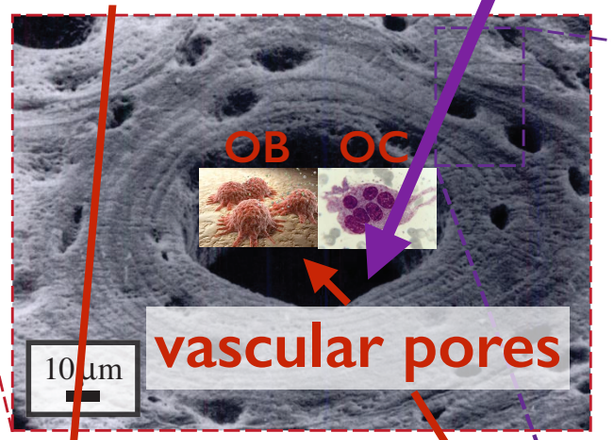
light micrograph of cortical bone[c]

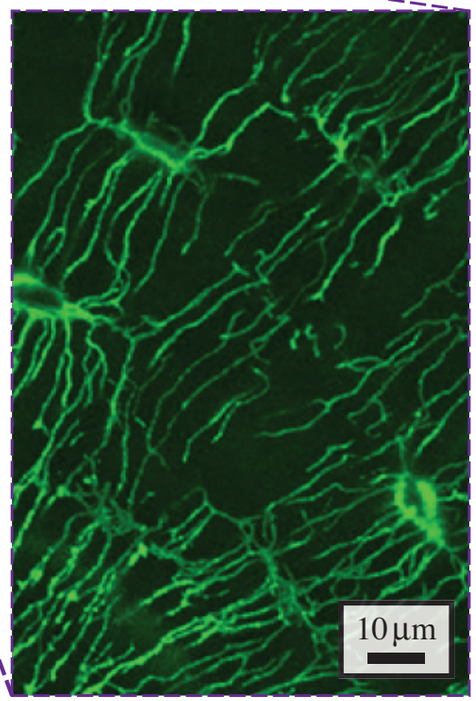


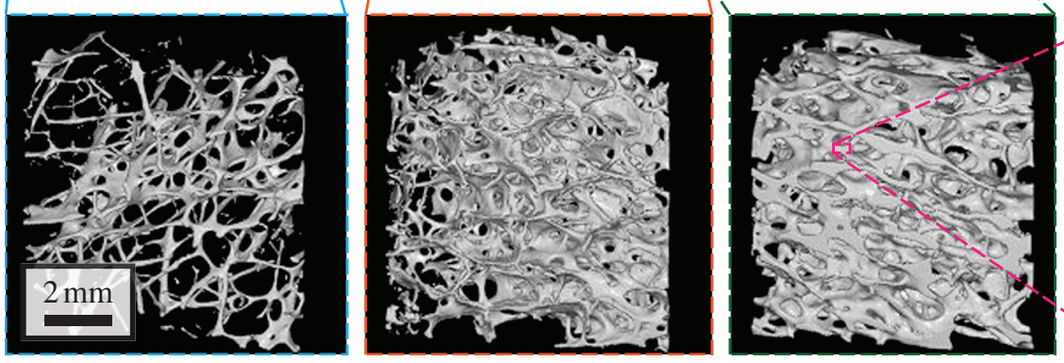
SEM image of an osteocyte[g]



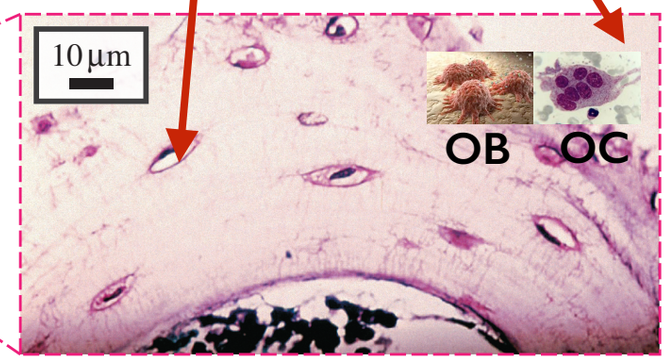
BIOLOGICAL FACTORS







CT-based reconstruction of trabecular bone[e]

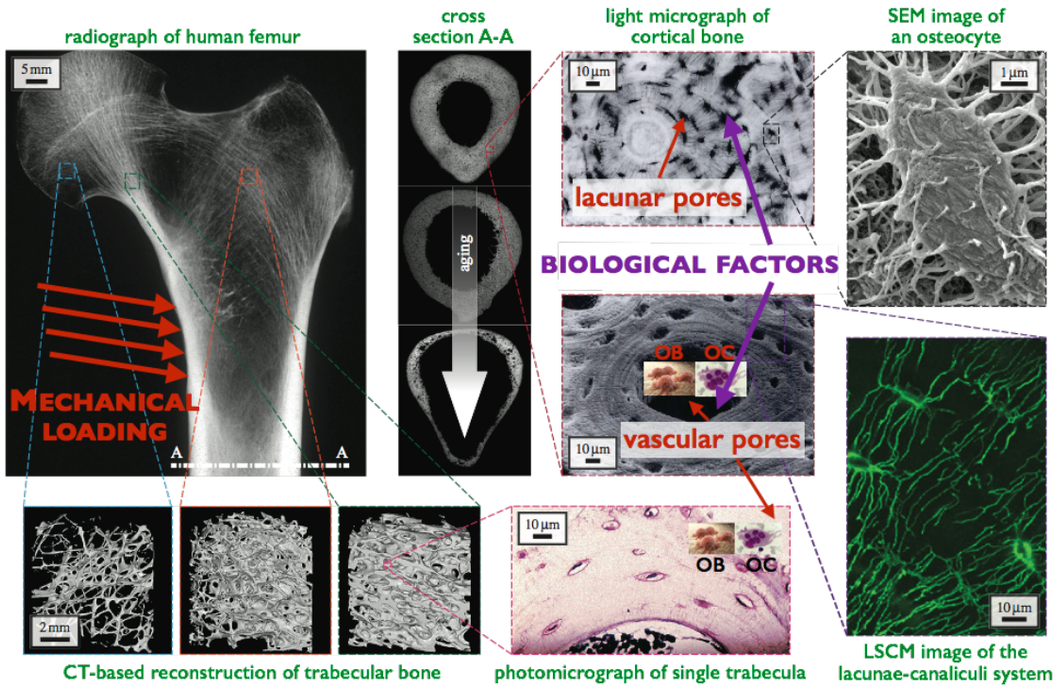


photomicrograph of single trabecula[f]

LSCM image of the lacunae-canaliculi system[h]

[a,f] Sinclair et al. (2013), *Equine Sports Medicine and Surgery*, pages 145-165, Saunders Ltd., second edition; [b] Melbourne Femur Collection, by courtesy of John G. Clement and David Thomas; [c] Buckwalter and Cooper (1987), *Instructional Course Lectures 36*, pages 27-48, American Academy of Orthopaedic Surgeons; [d] Kessel and Kardon (1979), *A Text-Atlas of Scanning Electron Microscopy*, W.H. Freeman & Co.; [e] Padilla et al. (2008), *Bone* 42: 1193-1202; [g] Pajevic (2009), *IBMS BoneKey* 6: 63-70; [h] Ebacher et al. (2012), *Acta Biomaterialia* 8: 1093-1100

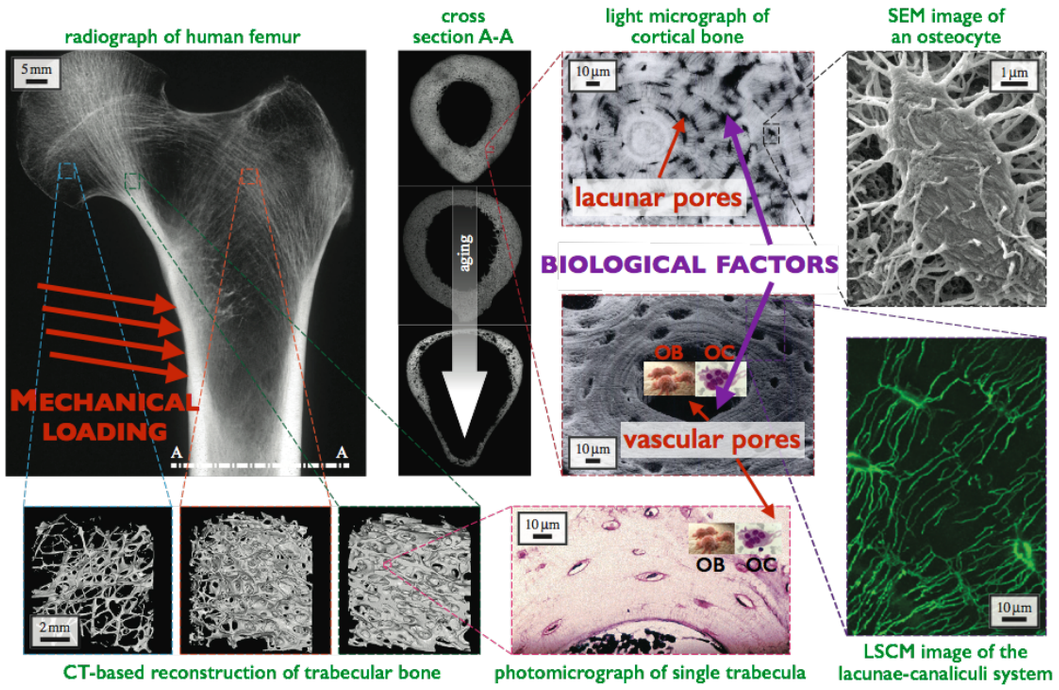
BONE REMODELING: PROBLEM DEFINITION



BONE REMODELING:

Interaction of osteoblasts, osteoclasts, and osteocytes, driven by biological factors and the mechanical loading

BONE REMODELING: PROBLEM DEFINITION



BONE REMODELING:

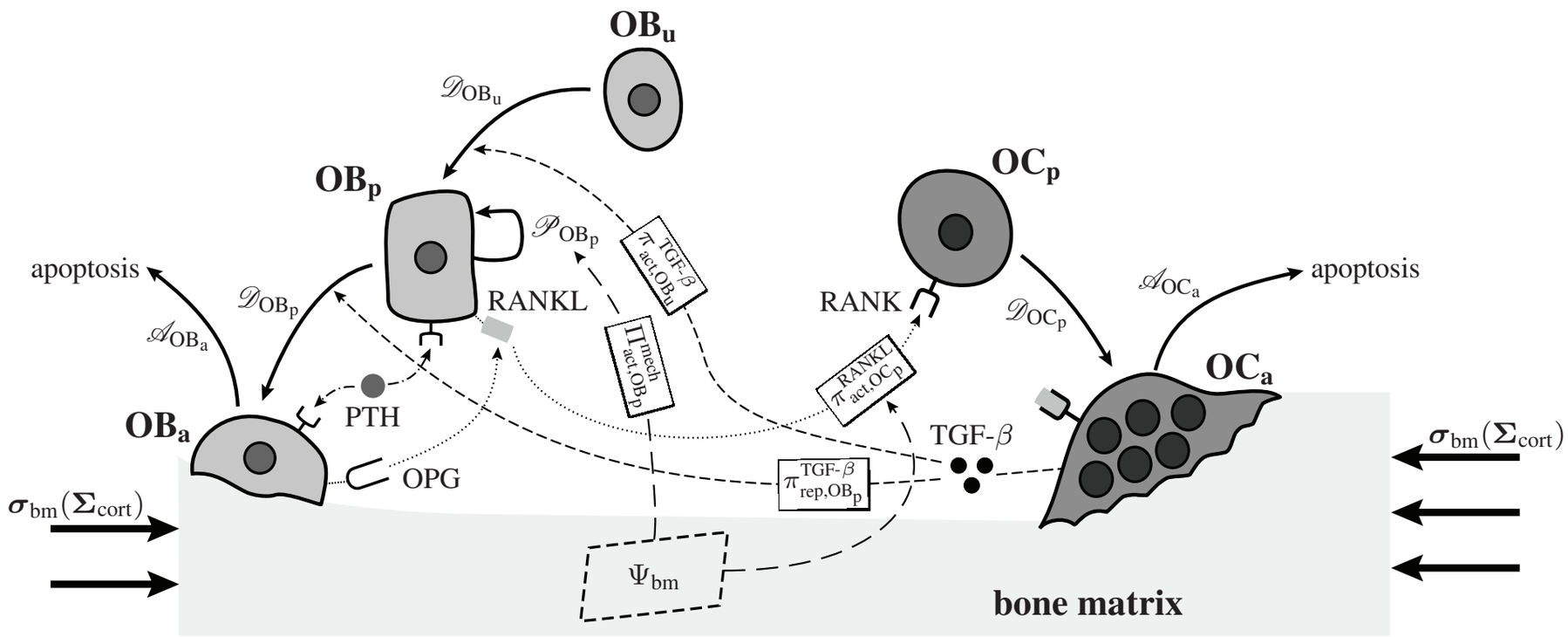
Interaction of osteoblasts, osteoclasts, and osteocytes, driven by biological factors and the mechanical loading

SPECIFIC AIMS:

- Development of a **multiscale systems biology model**;
- Taking into account the **major biochemical regulatory mechanisms**; and
- Fed by a **multiscale poromicromechanics** model, providing an **adequate mechanoregulatory stimulus**; for
- **Simulation of bone remodeling**-related bone composition changes due to **mechanical and pathological driving forces**

Bone Remodeling Simulation: Strategy

"Bone cell population model":



- Considers **osteoblasts and osteoclasts** in terms of **cell concentrations**;
- Takes into account **specific developmental stages** of these cells;
- Cell development through **differentiation, proliferation, and apoptosis** processes;
- Biochemical factors (RANK-RANKL-OPG, PTH, TGF-β) influence the cell development in terms of **activation and repression**.

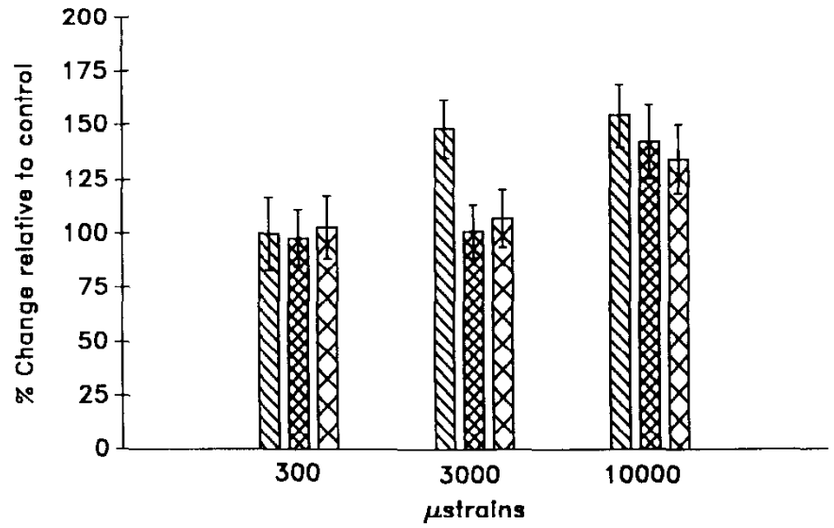
Lemaire et al. (2004), *Journal of Theoretical Biology* 229: 293-309; Pivonka et al. (2008), *Bone* 43: 249-316; Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196

Influence of Mechanical Loading

Osteoblast proliferation:

proliferation increase by **up to 100%**

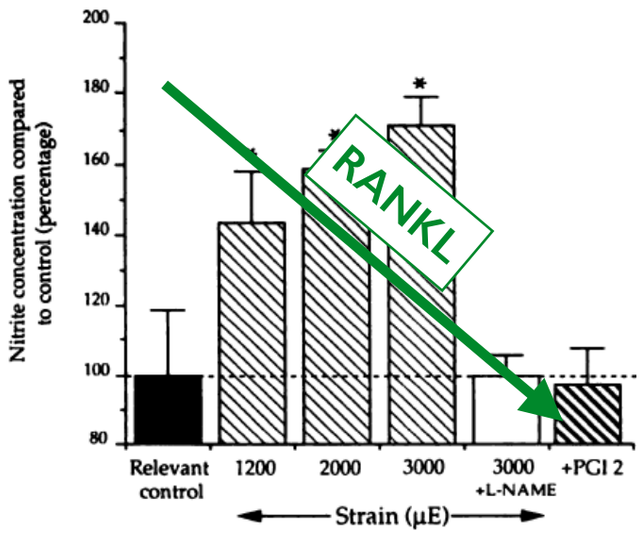
Jones et al. (1991), *Biomaterials* 12: 101-110



RANKL production:

Straining of bone matrix leads to increased NO-concentration, which is indicative for **restricted RANKL-production**

Pitsillides et al. (1995), *FASEB J* 9: 1614-1622; Xiong et al. (2011), *Nat Mater* 17: 1235-1241; Henriksen et al. (2003), *J Biol Chem* 278: 48745-48753, Wang et al. (2004), *Endocrinology* 145: 2148-2156



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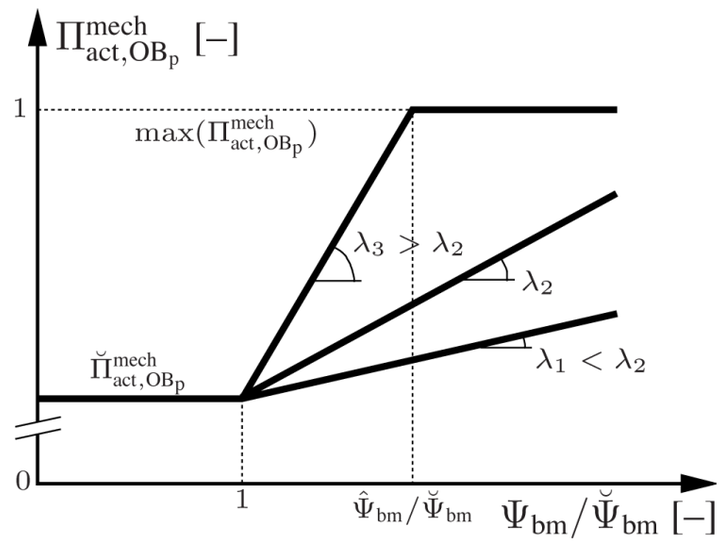

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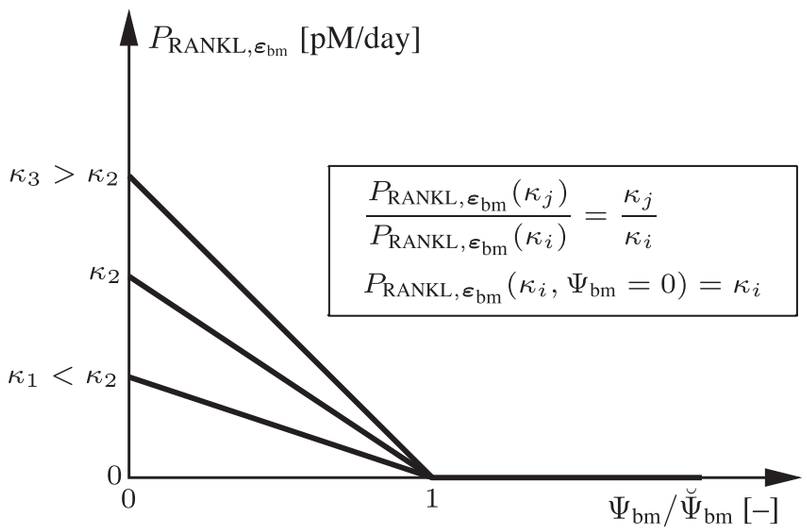

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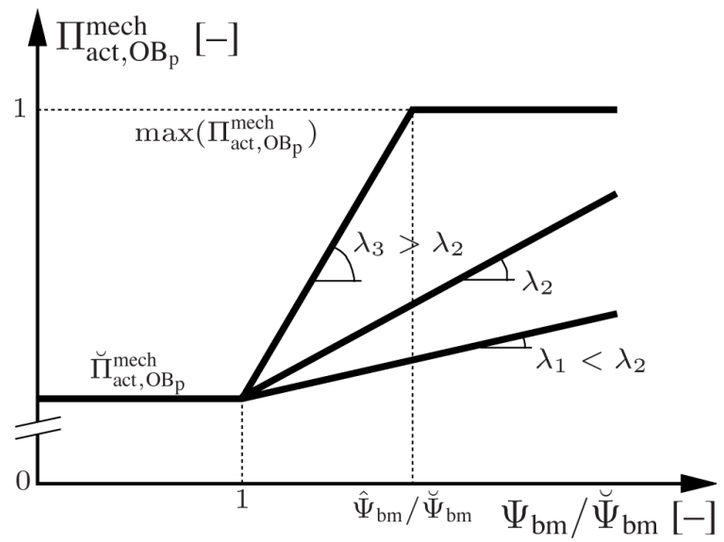

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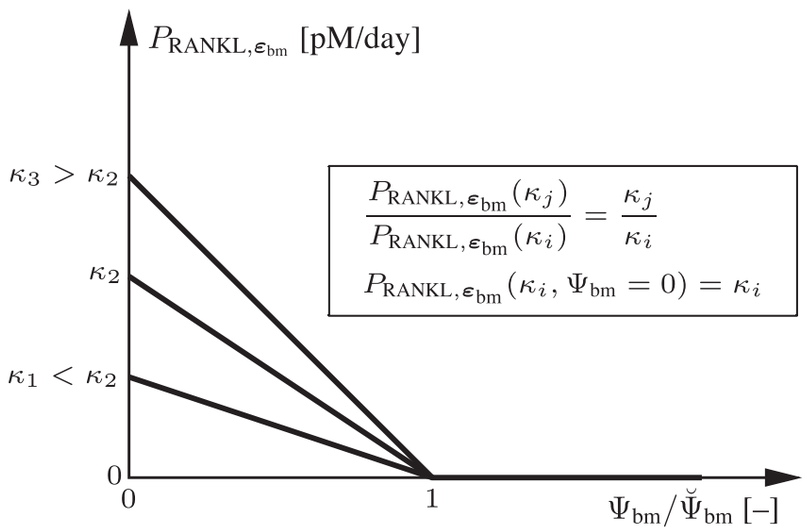

Mechanical stimulus:
- **SED** experienced by the **extravascular bone matrix**
- estimated by means of **continuum poromicromechanics**

Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196 ; Scheiner et al., *Biomechanics and Modeling in Mechanobiology*, available online; Pastrama et al., manuscript in preparation

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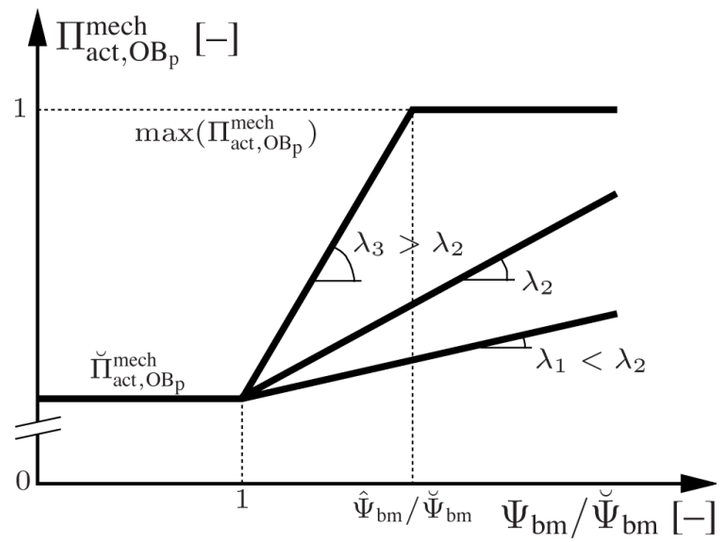

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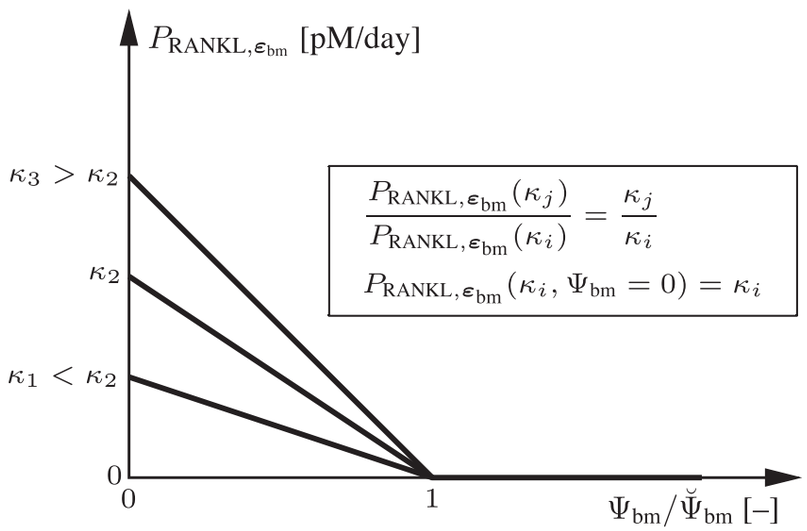


Mechanical stimulus:
- **hydrostatic pressures** experienced by bone cells
- estimated by means of **continuum poromicromechanics**

Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196 ; Scheiner et al., *Biomechanics and Modeling in Mechanobiology*, available online; Pastrama et al., manuscript in preparation

Bone Remodeling Simulation: Summary

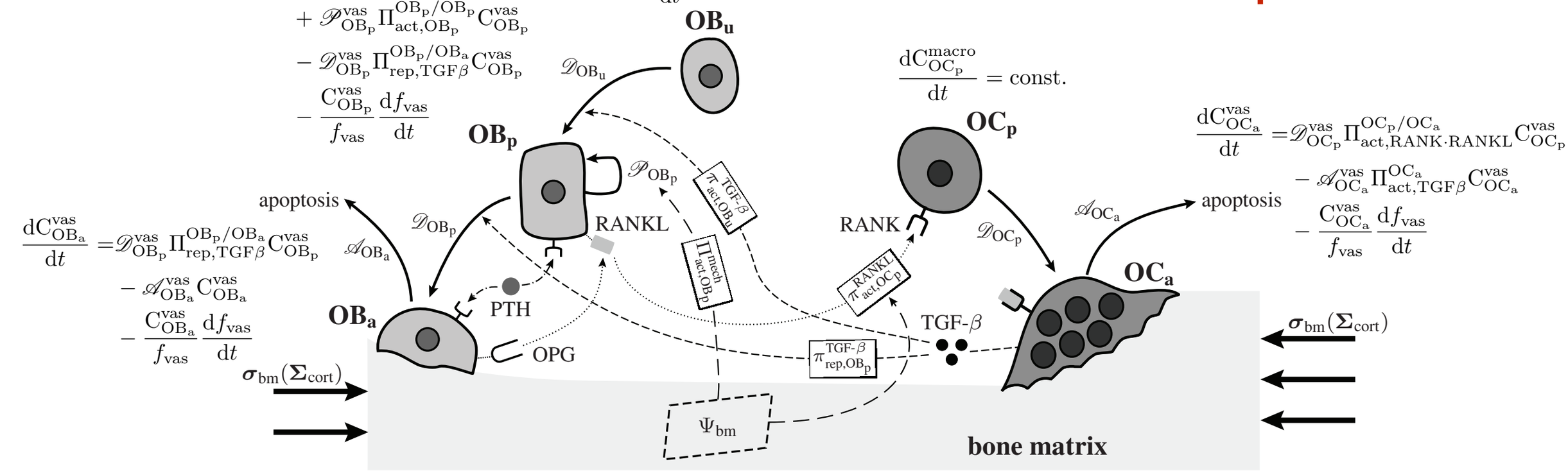
Set of 3 coupled ODEs

$$\frac{\mathrm{d}C^{\mathrm{vas}}_{\mathrm{OB_p}}}{\mathrm{d}t} = \mathscr{D}^{\mathrm{vas}}_{\mathrm{OB_u}} \Pi^{\mathrm{OB_u/OB_p}}_{\mathrm{act,TGF}\beta} C^{\mathrm{vas}}_{\mathrm{OB_u}} + \mathscr{P}^{\mathrm{vas}}_{\mathrm{OB_p}} \Pi^{\mathrm{OB_p/OB_p}}_{\mathrm{act,OB_p}} C^{\mathrm{vas}}_{\mathrm{OB_p}} - \mathscr{D}^{\mathrm{vas}}_{\mathrm{OB_p}} \Pi^{\mathrm{OB_p/OB_a}}_{\mathrm{rep,TGF}\beta} C^{\mathrm{vas}}_{\mathrm{OB_p}} - \frac{C^{\mathrm{vas}}_{\mathrm{OB_p}}}{f_{\mathrm{vas}}} \frac{\mathrm{d}f_{\mathrm{vas}}}{\mathrm{d}t}$$

$$\frac{\mathrm{d}C^{\mathrm{vas}}_{\mathrm{OB_a}}}{\mathrm{d}t} = \mathscr{D}^{\mathrm{vas}}_{\mathrm{OB_p}} \Pi^{\mathrm{OB_p/OB_a}}_{\mathrm{rep,TGF}\beta} C^{\mathrm{vas}}_{\mathrm{OB_p}} - \mathscr{A}^{\mathrm{vas}}_{\mathrm{OB_a}} C^{\mathrm{vas}}_{\mathrm{OB_a}} - \frac{C^{\mathrm{vas}}_{\mathrm{OB_a}}}{f_{\mathrm{vas}}} \frac{\mathrm{d}f_{\mathrm{vas}}}{\mathrm{d}t}$$

$$\frac{\mathrm{d}C^{\mathrm{vas}}_{\mathrm{OC_a}}}{\mathrm{d}t} = \mathscr{D}^{\mathrm{vas}}_{\mathrm{OC_p}} \Pi^{\mathrm{OC_p/OC_a}}_{\mathrm{act,RANK\cdot RANKL}} C^{\mathrm{vas}}_{\mathrm{OC_p}} - \mathscr{A}^{\mathrm{vas}}_{\mathrm{OC_a}} \Pi^{\mathrm{OC_a}}_{\mathrm{act,TGF}\beta} C^{\mathrm{vas}}_{\mathrm{OC_a}} - \frac{C^{\mathrm{vas}}_{\mathrm{OC_a}}}{f_{\mathrm{vas}}} \frac{\mathrm{d}f_{\mathrm{vas}}}{\mathrm{d}t}$$

$$\frac{\mathrm{d}C^{\mathrm{macro}}_{\mathrm{OB_u}}}{\mathrm{d}t} = \text{const.} \qquad \frac{\mathrm{d}C^{\mathrm{macro}}_{\mathrm{OC_p}}}{\mathrm{d}t} = \text{const.}$$



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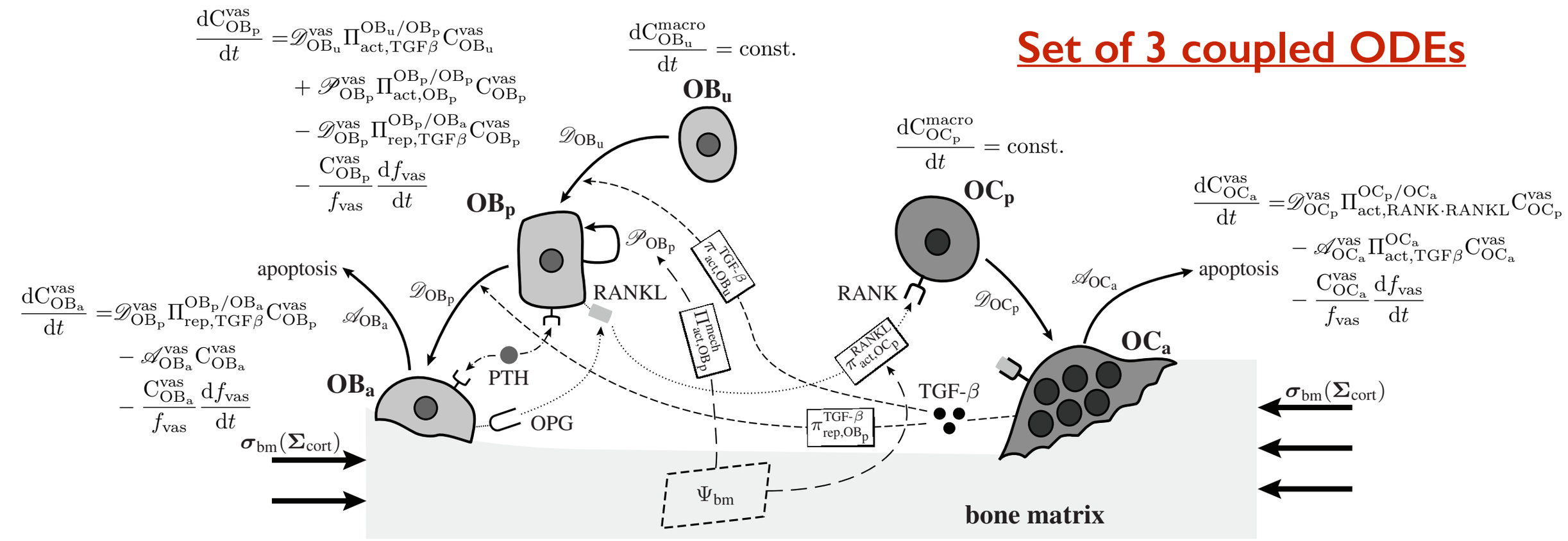

Set of 3 coupled ODEs

Relation to bone composition:

$$\frac{df_{vas}}{dt} = f_{vas}\left(C^{vas}_{OC_a} k^{vas}_{res} - C^{vas}_{OB_a} k^{vas}_{form}\right)$$

Volumetric bone **resorption** and **formation rates**

Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196 ; Scheiner et al., *Biomechanics and Modeling in Mechanobiology*, available online; Pastrama et al., manuscript in preparation

BONE REMODELING SIMULATION: SUMMARY

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$$\frac{\mathrm{dC}^{\mathrm{macro}}_{\mathrm{OB_u}}}{\mathrm{d}t} = \mathrm{const.}$$

$$\frac{\mathrm{dC}^{\mathrm{macro}}_{\mathrm{OC_p}}}{\mathrm{d}t} = \mathrm{const.}$$

$$\frac{\mathrm{dC}^{\mathrm{vas}}_{\mathrm{OC_a}}}{\mathrm{d}t} = \mathscr{D}^{\mathrm{vas}}_{\mathrm{OC_p}} \Pi^{\mathrm{OC_p/OC_a}}_{\mathrm{act,RANK\cdot RANKL}} \mathrm{C}^{\mathrm{vas}}_{\mathrm{OC_p}} - \mathscr{A}^{\mathrm{vas}}_{\mathrm{OC_a}} \Pi^{\mathrm{OC_a}}_{\mathrm{act,TGF}\beta} \mathrm{C}^{\mathrm{vas}}_{\mathrm{OC_a}} - \frac{\mathrm{C}^{\mathrm{vas}}_{\mathrm{OC_a}}}{f_{\mathrm{vas}}} \frac{\mathrm{d}f_{\mathrm{vas}}}{\mathrm{d}t}$$

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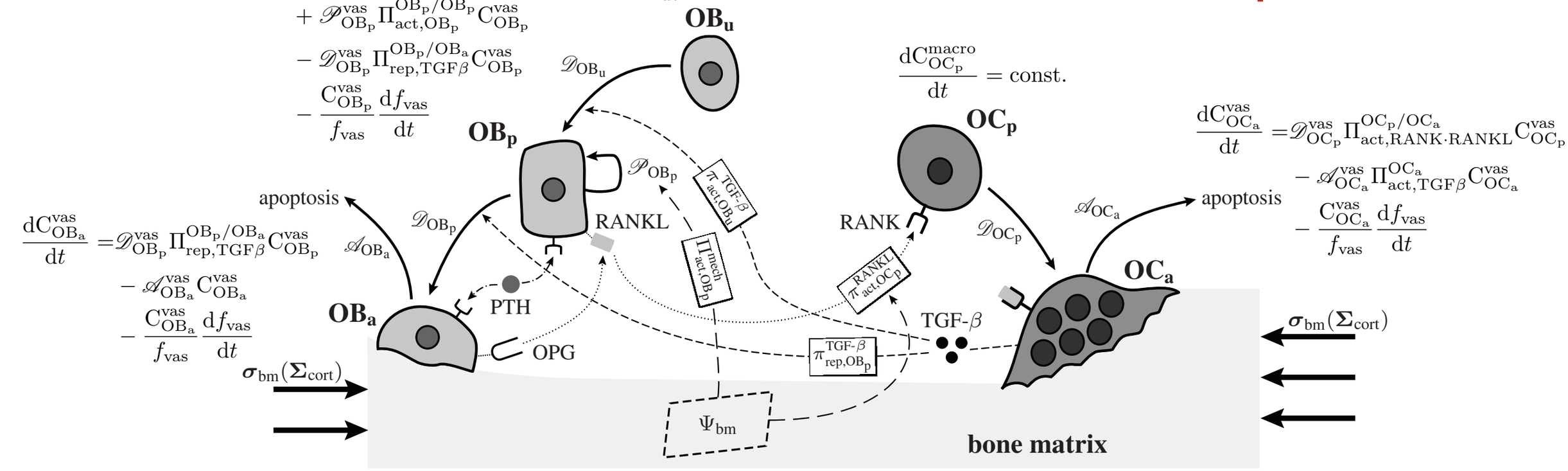

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RELATION TO BONE COMPOSITION:

$$\frac{\mathrm{d}f_{\mathrm{vas}}}{\mathrm{dt}} = f_{\mathrm{vas}} \left(\mathrm{C}^{\mathrm{vas}}_{\mathrm{OC_a}} k^{\mathrm{vas}}_{\mathrm{res}} - \mathrm{C}^{\mathrm{vas}}_{\mathrm{OB_a}} k^{\mathrm{vas}}_{\mathrm{form}} \right)$$

Volumetric bone **resorption** and **formation rates**

FEEDBACK-TYPE INTERPLAY BETWEEN BONE BIOLOGY AND BONE MECHANICS!

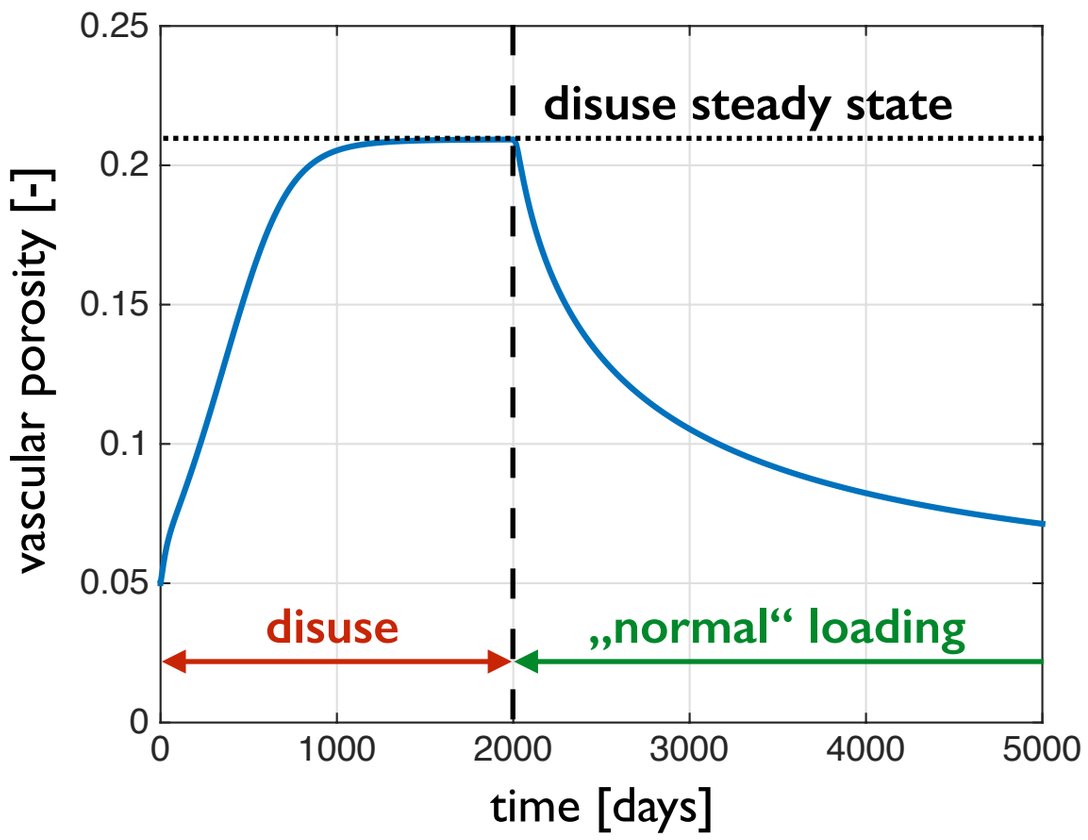
Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196 ; Scheiner et al., *Biomechanics and Modeling in Mechanobiology*, available online; Pastrama et al., manuscript in preparation

Simulation of Mechanical Disuse

Temporary prescription of **decreased macroscopic loading**:

$$\boldsymbol{\Sigma}_{\text{cort}}^{\text{norm}} = -\begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 30 \end{bmatrix} \text{MPa}$$

$$\boldsymbol{\Sigma}_{\text{cort}}^{\text{disuse}} = -\begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 25 \end{bmatrix} \text{MPa}$$



- ✓ Resulting **bone loss rate (0.61%/month) agrees well with clinical data**
  Vico et al. (1992), *Journal of Bone and Mineral Research* 7: 445-447; Vico et al. (2000), *Lancet* 355: 1607-1611
- ✓ According to clinical studies, **bone loss varies between different species**, calling for species-specific model calibration

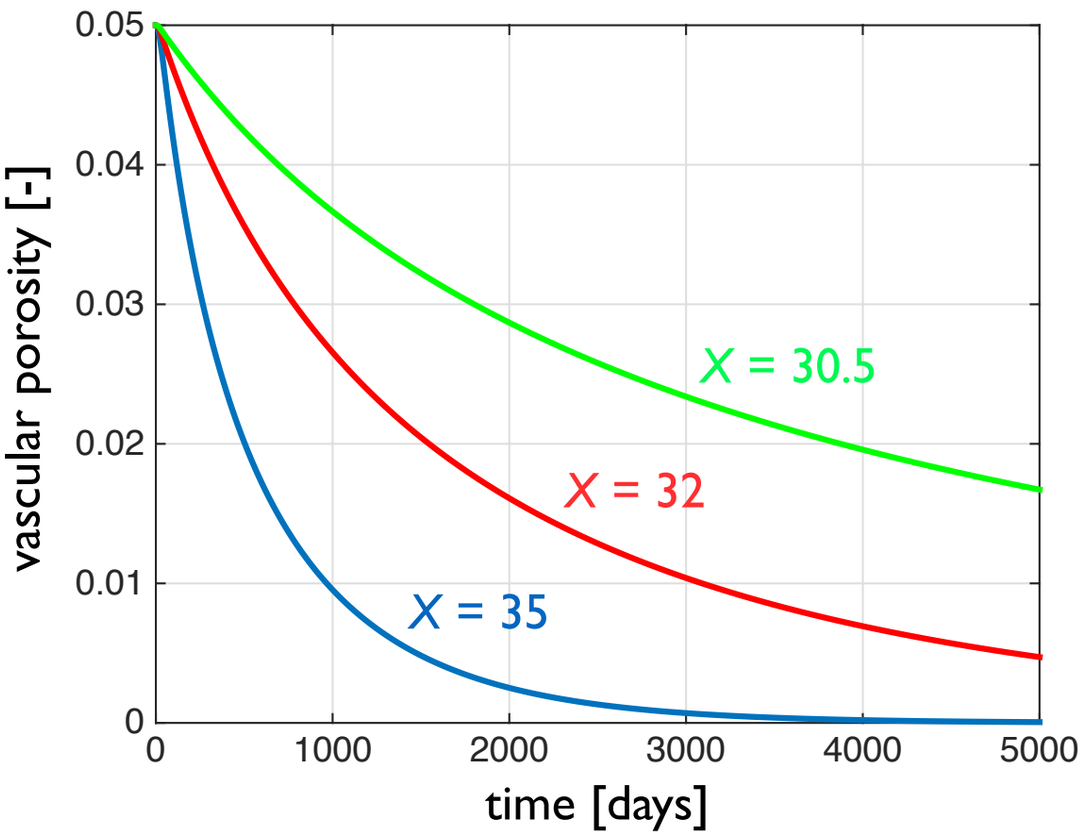
Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196; Pastrama et al., manuscript in preparation

Simulation of Mechanical Overuse

Prescription of **increased macroscopic loading**:

$$\boldsymbol{\Sigma}_{\text{cort}}^{\text{norm}} = -\begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 30 \end{bmatrix} \text{MPa}$$

$$\boldsymbol{\Sigma}_{\text{cort}}^{\text{disuse}} = -\begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & X \end{bmatrix} \text{MPa}$$



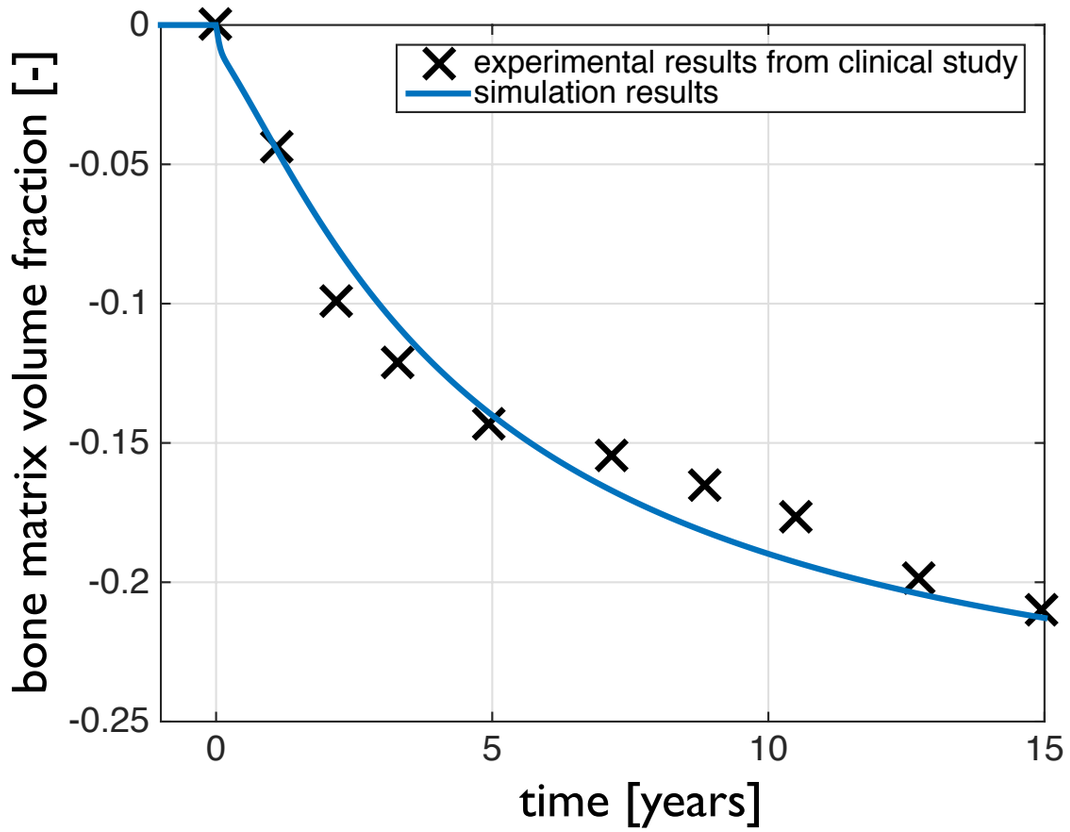
- ✓ Bone gain depends on magnitude of overuse: **higher magnitudes lead to faster and more significant bone gain**
- ✓ The multiscale systems biology approach implies that **bone gain is limited**

Scheiner et al. (2013), *Computer Methods in Applied Mechanics and Engineering* 254: 181-196; Pastrama et al., manuscript in preparation

Simulation of Osteoporosis

Prescription of **disease-related, temporary increase of RANKL and osteocyte apoptosis**

Manolagas (2000), *Endocr Rev* 21: 115-137; Hofbauer and Schoppet (2004), *J Am Med Assoc* 292: 490-495; Tomkinson et al. (1998), *J Bone Miner Res* 13: 1243-1250



- ✓ onset of PMO leads to a **catabolic bone remodeling regime**
- ✓ adequate **bone turnover kinetics**
- ✓ the **related porosity increase** agrees well with clinical results
- ✓ **drug intervention** can be modeled through consideration of adequate pharmacokinetics models

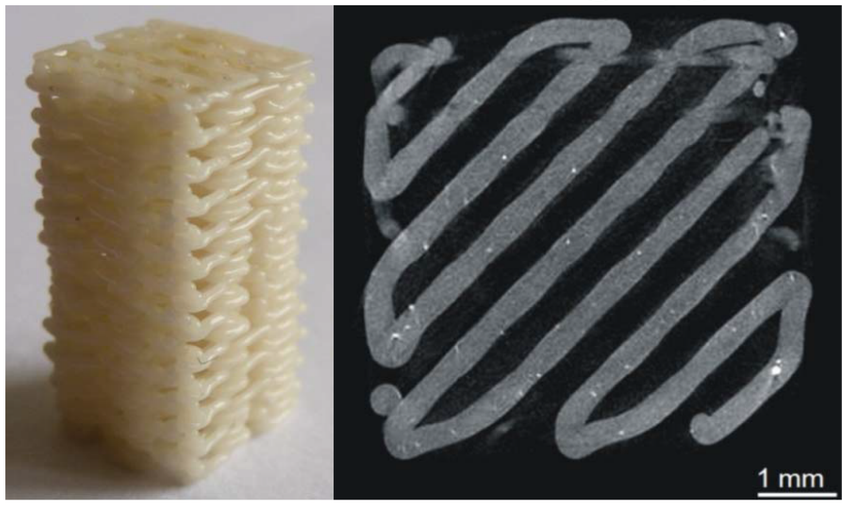
Scheiner et al. (2014), *International Journal of Numerical Methods in Biomedical Engineering* 30: 1-27; Pastrama et al., manuscript in preparation

MODELING: SUMMARY

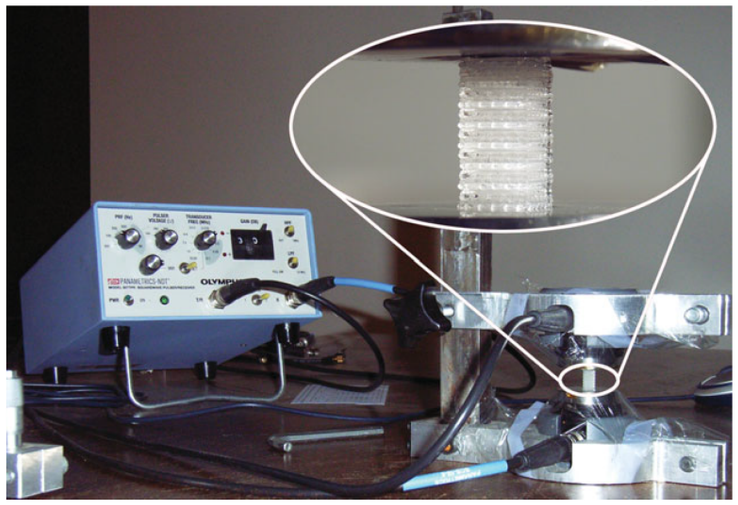
- ✓ Adequate **prediction of various mechanical properties** of bone tissue and of specific biomaterials
- ✓ **Structural simulations of bone organs**, using micromechanics-derived material properties as input
- ✓ Conversion of **CT data to** voxel-specific constituent **volume fractions**
- ✓ **Estimation of bone remodeling-modulating mechanical stimuli** through rigorous multiscale poromicromechanical modeling
- ✓ Adequate **simulation of bone remodeling** (on the material level) mechanical and biological load cases

EXPERIMENTS@IMWS

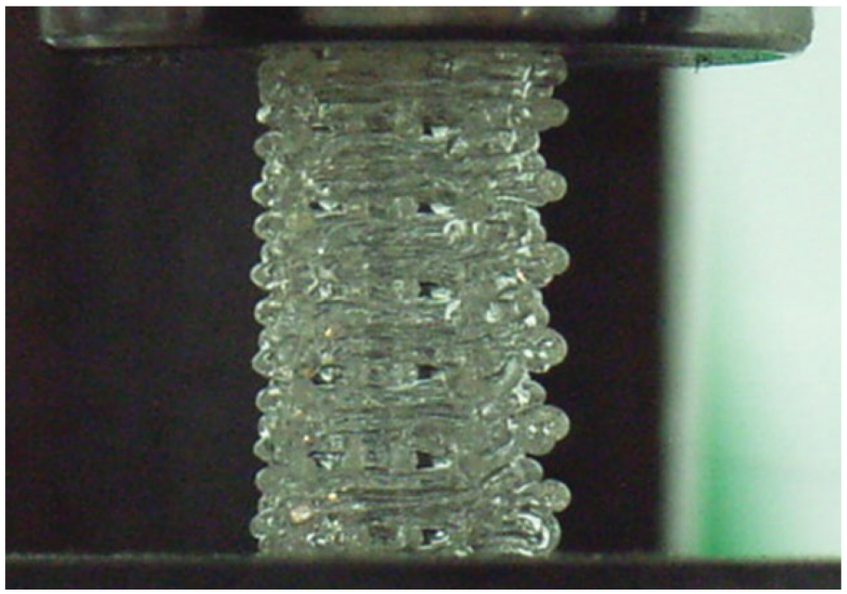
microCT imaging



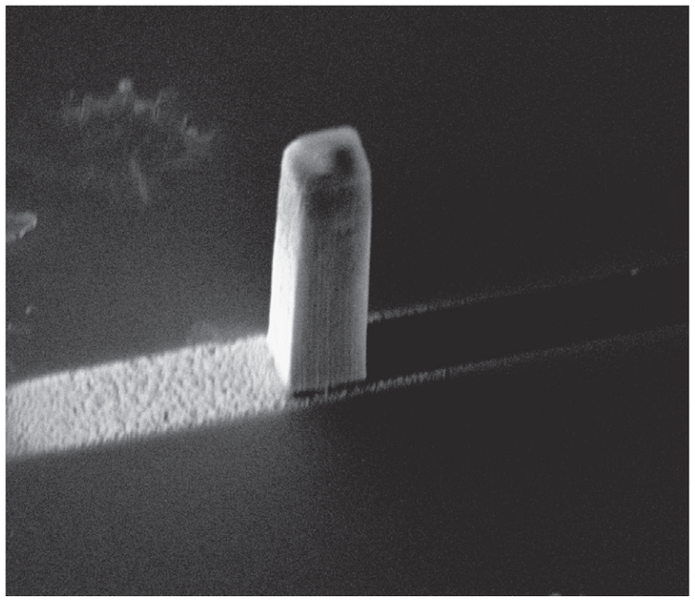
ultrasonics testing



Uniaxial loading-unloading tests



micropillar tests



…plus classical macroscopic mechanical testing, nano- and pico-indentation, atomic force microscopy, scanning probe microscopy

Luczynski et al. (2012), *CMES-Computer Modeling in Engineering & Sciences* 87: 505-528; Luczynski et al. (2013), *Journal of Biomedical Materials Research Part A* 101A: 138-144; Hum et al. (2013), *Strain* 49: 431-439, Luczynski et al. (2015), *Journal of the Mechanical Behavior of Biomedical Materials*, available online

Thank you for your Attention!

stefan.scheiner@tuwien.ac.at

Multiscale poromicromechanics of bone materials, with links to biology and medicine

Saskatchewan-CHIR Partnership Program

Multi-scale modeling of transport through deformable porous materials

Russian Science Foundation

Functional prognosis simulation of patient-specific spinal treatment for clinical use

Simulation Tool for Bone and Bone Biomaterials, based on Enhanced CT-Data Exploitation