frontiers

Supplementary Material: Multiscale modeling provides differentiated insights to fluid flow-driven stimulation of bone cellular activities

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Bone: Organic/Inorganic Matter Architecture and Mechanics

PRELIMINARY REMARKS

In the following, equations referred to by Arabic numbers plus the letter "S" in front relate to the Supplementary Material, while equations referred to by Arabic numbers only relate to the main paper.

1 TRANSFORMATION RULES FOR SECOND-ORDER TENSORS

Several of the second-order tensors occurring in this work relate to cylindrical pores, with the latter being oriented arbitrarily in space, as for instance the inhomogeneity tensor $\mathbf{P}_{\text{can}}^{\text{exlac}}$, defined in Eq. (14). The orientation is defined in spherical coordinates, by means of the Euler angles ϑ and φ. In order to get the components of these quantities in Cartesian coordinates, as functions of ϑ and φ, the standard transformation rule for second-order tensors (Salençon, 2001) is applied, reading (for the example of inhomogeneity tensor $\mathbf{P}_{\text{can}}^{\text{exlac}}$) as

$$\mathbf{P}_{\text{can}}^{\text{exlac}}(\vartheta,\varphi) = \mathbf{Q}\cdot\mathbf{P}_{\text{can}}^{\text{exlac}}\cdot\mathbf{Q}^{\text{T}}\,, \tag{S1}$$

with the transformation matrix $\mathbf{Q}$ defined as

$$\mathbf{Q} = \begin{pmatrix} \sin\vartheta\,\cos\varphi & \cos\vartheta\,\cos\varphi & -\sin\varphi \\ \sin\vartheta\,\sin\varphi & \cos\vartheta\,\sin\varphi & \cos\varphi \\ \cos\vartheta & -\sin\vartheta & 0 \end{pmatrix}. \tag{S2}$$

2 RESULTING CONCENTRATION AND PERMEABILITY TENSORS

In order to keep the subsequently presented equations as concise and compact as possible, the following auxiliary variables are introduced:

$$\begin{gathered} \alpha_1 = \phi_{\text{can}}^{\text{exlac}} + 9\,, \quad \alpha_2 = \phi_{\text{lac}}^{\text{exvas}} + 2\,, \quad \alpha_3 = \phi_{\text{lac}}^{\text{exvas}} - 1\,, \quad \alpha_4 = \phi_{\text{vas}}^{\text{macro}} + 9\,, \\ \alpha_5 = 14\phi_{\text{vas}}^{\text{macro}} - 9\,, \quad \alpha_6 = 16\phi_{\text{vas}}^{\text{macro}} + 9\,, \quad \alpha_7 = 4\phi_{\text{vas}}^{\text{macro}} - 9\,, \quad \alpha_8 = 13\phi_{\text{vas}}^{\text{macro}} - 18\,, \end{gathered} \tag{S3}$$

and

$$\beta_1 = \frac{9\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2}{2\alpha_1 r_{\text{lac}}^2 + 6\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2}\,, \quad \beta_2 = \frac{6\phi_{\text{lac}}^{\text{exvas}} r_{\text{lac}}^2}{3\alpha_2\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - 2\alpha_1\alpha_3 r_{\text{lac}}^2}\,,$$

$$\beta_3 = \frac{1-\phi_{\text{lac}}^{\text{exvas}}}{\alpha_1\left[(\beta_1-1)\phi_{\text{lac}}^{\text{exvas}}+1\right]} + \beta_2\,, \tag{S4}$$

$$\beta_4 = \sqrt{8\alpha_4\beta_3\phi_{\text{can}}^{\text{exlac}}\phi_{\text{vas}}^{\text{macro}} r_{\text{can}}^2 r_{\text{vas}}^2 + \left(2\alpha_5\beta_3\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - 2\phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)^2}\,.$$

2.1 ON THE RVE OF EXTRALACUNAR BONE MATRIX

Insertion of Eqs. (14) – (16), as well as of $\mathbf{K}_{\text{excan}} = 0$, into Eqs. (12) and (13) yields the concentration tensors of the canalicular pores, $\mathbf{A}_{\text{can}}(\vartheta,\varphi)$, and of extracanalicular bone matrix, $\mathbf{A}_{\text{excan}}$, reading as

$$\mathbf{A}_{\text{can}}(\vartheta,\varphi) = \begin{pmatrix} A_{\text{can},11}(\vartheta,\varphi) & A_{\text{can},12}(\vartheta,\varphi) & A_{\text{can},13}(\vartheta,\varphi) \\ A_{\text{can},21}(\vartheta,\varphi) & A_{\text{can},22}(\vartheta,\varphi) & A_{\text{can},23}(\vartheta,\varphi) \\ A_{\text{can},31}(\vartheta,\varphi) & A_{\text{can},32}(\vartheta,\varphi) & A_{\text{can},33}(\vartheta,\varphi) \end{pmatrix}\,, \tag{S5}$$

with components

$$A_{\text{can},11}(\vartheta,\varphi) = \frac{3}{2\alpha_1}\left(2\cos^2\varphi\,\cos 2\vartheta - \cos 2\varphi + 7\right)\,, \tag{S6}$$

$$A_{\text{can},22}(\vartheta,\varphi) = \frac{3}{2\alpha_1}\left(2\sin^2\varphi\,\cos 2\vartheta + \cos 2\varphi + 7\right)\,, \tag{S7}$$

$$A_{\text{can},33}(\vartheta,\varphi) = \frac{1}{\alpha_1}\left(9 - 3\cos 2\vartheta\right)\,, \tag{S8}$$

$$A_{\text{can},12}(\vartheta,\varphi) = -\frac{1}{\alpha_1}\left(3\sin 2\varphi\,\sin^2\vartheta\right) = A_{\text{can},21}(\vartheta,\varphi)\,, \tag{S9}$$

$$A_{\text{can},13}(\vartheta,\varphi) = -\frac{1}{\alpha_1}\left(6\cos\varphi\,\sin\vartheta\,\cos\vartheta\right) = A_{\text{can},13}(\vartheta,\varphi)\,, \tag{S10}$$

$$A_{\text{can},23}(\vartheta,\varphi) = -\frac{1}{\alpha_1}\left(6\sin\varphi\,\sin\vartheta\,\cos\vartheta\right) = A_{\text{can},23}(\vartheta,\varphi)\,, \tag{S11}$$

and

$$\mathbf{A}_{\text{excan}} = \frac{9}{\alpha_1}\mathbf{1}\,, \tag{S12}$$

The permeability tensor of extralacunar bone matrix follows from insertion of Eqs. (S5) – (S12) into Eq. (17),

$$K_{\text{exlac}} = \frac{\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2}{4\alpha_1\eta}\mathbf{1}\,. \tag{S13}$$

2.2 ON THE RVE OF EXTRAVASCULAR BONE MATRIX

Insertion of Eqs. (15), (22), and (S13) into Eqs. (20) and (21) yields the concentration tensors of the lacunar pores, $\mathbf{A}_{\text{lac}}$, and of the extralacunar bone matrix, $\mathbf{A}_{\text{exlac}}$, reading as

$$\mathbf{A}_{\text{lac}} = \frac{9\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2}{3\alpha_2\phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - 2\alpha_1\alpha_3 r_{\text{lac}}^2}\mathbf{1}\,, \tag{S14}$$

and

$$\mathbf{A}_{\text{exlac}} = \frac{1}{1 + (\beta_1 - 1)\phi_{\text{lac}}^{\text{exvas}}} \mathbf{1} \,. \tag{S15}$$

The permeability tensor of extravascular bone matrix follows from insertion of Eqs. (S14) and (S15) into Eq. (23),

$$K_{\text{exvas}} = \frac{\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2}{4\eta} \mathbf{1} \,. \tag{S16}$$

2.3 ON THE RVE OF MACROSCOPIC BONE TISSUE WITH ARBITRARILY ORIENTED VASCULAR PORES

Inserting Eqs. (28) – (30) into Eqs. (26) and (27) yields, when considering macroscopic bone tissue with arbitrarily oriented vascular pores, the concentration tensors of vascular pores, $\mathbf{A}_{\text{vas}}^{\text{arb}}(\vartheta, \varphi)$, and of extravascular bone matrix, $\mathbf{A}_{\text{exvas}}^{\text{arb}}$, reading as

$$\mathbf{A}_{\text{vas}}^{\text{arb}}(\vartheta, \varphi) = \begin{pmatrix} A_{\text{vas},11}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},12}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},13}^{\text{arb}}(\vartheta, \varphi) \\ A_{\text{vas},21}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},22}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},23}^{\text{arb}}(\vartheta, \varphi) \\ A_{\text{vas},31}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},32}^{\text{arb}}(\vartheta, \varphi) & A_{\text{vas},33}^{\text{arb}}(\vartheta, \varphi) \end{pmatrix} , \tag{S17}$$

with components

$$A_{\text{vas},11}^{\text{arb}}(\vartheta, \varphi) = \frac{9\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 \left(2\cos^2\varphi \, \cos 2\vartheta - \cos 2\varphi + 7\right)}{2\left(\alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \beta_4 - \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)} , \tag{S18}$$

$$A_{\text{vas},22}^{\text{arb}}(\vartheta, \varphi) = \frac{9\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 \left(2\sin^2\varphi \, \cos 2\vartheta + \cos 2\varphi + 7\right)}{2\left(\alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \beta_4 - \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)} , \tag{S19}$$

$$A_{\text{vas},33}^{\text{arb}}(\vartheta, \varphi) = \frac{9\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 (3 - \cos 2\vartheta)}{\alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \beta_4 - \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2} , \tag{S20}$$

$$A_{\text{vas},12}^{\text{arb}}(\vartheta, \varphi) = \frac{3\,\sin 2\varphi \, \sin^2\vartheta \left(\beta_4 - \alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)}{2\alpha_4 \phi_{\text{vas}}^{\text{macro}} \left(10\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - r_{\text{vas}}^2\right)} = A_{\text{vas},21}^{\text{arb}}(\vartheta, \varphi) \,, \tag{S21}$$

$$A_{\text{vas},13}^{\text{arb}}(\vartheta, \varphi) = \frac{3\cos\varphi \, \sin 2\vartheta \left(\beta_4 - \alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)}{2\alpha_4 \phi_{\text{vas}}^{\text{macro}} \left(10\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - r_{\text{vas}}^2\right)} = A_{\text{vas},31}^{\text{arb}}(\vartheta, \varphi) \,, \tag{S22}$$

$$A_{\text{vas},23}^{\text{arb}}(\vartheta, \varphi) = \frac{3\sin\varphi \, \sin 2\vartheta \left(\beta_4 - \alpha_6 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2\right)}{2\alpha_4 \phi_{\text{vas}}^{\text{macro}} \left(10\beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - r_{\text{vas}}^2\right)} = A_{\text{vas},32}^{\text{arb}}(\vartheta, \varphi) \,, \tag{S23}$$

and

$$A_{\text{exvas}}^{\text{arb}} = \frac{9 r_{\text{vas}}^2}{\alpha_7 r_{\text{vas}}^2 - 5\alpha_5 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 - 5\beta_4} \,. \tag{S24}$$

The permeability tensor of macroscopic bone tissue containing arbitrarily oriented vascular pores follows from insertion of Eqs. (S17) – (S24) into Eq. (31),

$$K_{\text{macro}}^{\text{arb}} = \frac{1}{8\alpha_4 \eta} \Bigg(\sqrt{\alpha_5^2 \beta_3^2 (\phi_{\text{can}}^{\text{exlac}})^2 r_{\text{can}}^4 - 2\alpha_8 \beta_3 \phi_{\text{can}}^{\text{exlac}} \phi_{\text{vas}}^{\text{macro}} r_{\text{can}}^2 r_{\text{vas}}^2 + (\phi_{\text{vas}}^{\text{macro}})^2 r_{\text{vas}}^4} - \alpha_5 \beta_3 \phi_{\text{can}}^{\text{exlac}} r_{\text{can}}^2 + \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2 \Bigg) \,. \tag{S25}$$

2.4 ON THE RVE OF MACROSCOPIC BONE TISSUE WITH LONGITUDINALLY ORIENTED VASCULAR PORES

Inserting Eqs. (39), (36), and (S16) into Eqs. (34) and (35) yields, when considering macroscopic bone tissue with longitudinally oriented vascular pores, the concentration tensors of vascular pores, $\mathbf{A}_{\text{vas}}^{\text{long}}$, and of extravascular bone matrix, $\mathbf{A}_{\text{exvas}}^{\text{long}}$, reading as

$$\mathbf{A}_{\text{vas}}^{\text{long}} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \dfrac{2}{\phi_{\text{vas}}^{\text{macro}} + 1} & 0 \\ 0 & 0 & \dfrac{2}{\phi_{\text{vas}}^{\text{macro}} + 1} \end{pmatrix} , \tag{S26}$$

and

$$\mathbf{A}_{\text{exvas}}^{\text{long}} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \dfrac{1}{\phi_{\text{vas}}^{\text{macro}} + 1} & 0 \\ 0 & 0 & \dfrac{1}{\phi_{\text{vas}}^{\text{macro}} + 1} \end{pmatrix} . \tag{S27}$$

The permeability tensor of macroscopic bone tissue containing longitudinally oriented vascular pores follows from insertion of Eqs. (S26) and (S27) into Eq. (37),

$$\mathbf{K}_{\text{macro}}^{\text{long}} = K_{\text{macro}}^{\text{long,long}} \mathbf{e}_{\text{s}} \otimes \mathbf{e}_{\text{s}} + K_{\text{long,trans}}^{\text{long,trans}} \mathbf{e}_{\text{t}} \otimes \mathbf{e}_{\text{t}} + K_{\text{macro}}^{\text{long,trans}} \mathbf{e}_{\text{u}} \otimes \mathbf{e}_{\text{u}} , \tag{S28}$$

with components

$$K_{\text{macro}}^{\text{long,long}} = \frac{2\beta_3 \phi_{\text{can}}^{\text{exlac}} (1 - \phi_{\text{vas}}^{\text{macro}}) r_{\text{can}}^2 + \phi_{\text{vas}}^{\text{macro}} r_{\text{vas}}^2}{8\eta} , \tag{S29}$$

and

$$K_{\text{macro}}^{\text{long,trans}} = \frac{\beta_3 \phi_{\text{can}}^{\text{exlac}} (1 - \phi_{\text{vas}}^{\text{macro}}) r_{\text{can}}^2}{4\eta (\phi_{\text{vas}}^{\text{macro}} + 1)} . \tag{S30}$$

REFERENCES

Salençon J. *Handbook of Continuum Mechanics* (Springer-Verlag Berlin Heidelberg) (2001).