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## Homogenization of advection-diffusion and solid diffusion in poroelastic media for modelling transport of soluble factors in biological tissues

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This work has been motivated by the study of solid tumor growth and more specifically by the examination of the most frequent pediatric primary bone tumors (osteosarcoma), which are characterised in their early stage by the formation of non-mineralised bone tissue, called osteoid [1]. As the tumor evolves in time, mineralisation of this growing tissue can take place. The purpose of this work thus is to investigate the advection-diffusion of soluble factor such as calcium and phosphate [2] in the context of tumor mineralisation, how this mineralisation of bone tissue may become a barrier to treatment in the context of drug transport [3] but also how proteins and growth factors can play a role in tumor growth [4]. For this purpose, the method of asymptotic homogenization is used so as to derive the macroscopic models for describing solute transport in poroelastic media, with an advective-diffusive regime in the fluid-saturated pores and diffusion in the solid phase, by starting from the description on the pore scale. The fluid/solid equations lead to Biot's model of poroelasticity. Then, homogenization of the transport equations leads to three macroscopic models that relate to three orders of magnitude of the diffusivity ratio: a model in which the solid diffusion only influences the accumulation term; ii) a model with memory effects; iii) a model without solid diffusion. Initially expressed by means of orders of magnitude of the diffusivity ratio, the domains of validity of each of these three models can be expressed in terms of relative orders of magnitude of two characteristic times. The three models contain a solute-solid interaction term, due to the advection regime and they are coupled to the porcelaticity model via the advection term.

[1] Fletcher, C. D.M., Bridge, J.A., Hogendoorn, P., Mertens, F. (2013): WHO Classification of Tumours of Soft Tissue and Bone, Volume 5.

[2] Giacaman, R., Perez, V., Carrera, C. (2016): Mineralization processes in hard tissues, Biomineralization and Biomaterials, 147-185.

[4] Ambard, D., Swider, P. (2006): A predictive mechano-biological model of the bone-implant healing, European Journal of Mechanics - A/Solids. 25. 927-937.

<sup>[3]</sup> Sciumè, G., Shelton, S.E., Gray, W.G.T, Millers, C., Hussain, F., Ferrari, M., Decuzzi, P., Schrefler, B. (2012): Tumor growth modelling from the perspective of porous media mechanics, Molecular and cellular biomechanics : MCB. 9. 193-212.