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A Multiscale and Multiphase Model for the Description of Growth Effects and Hepatotoxicity in the Human Liver

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The liver is the most important human organ responsible for metabolic homeostatis. A further central task of the human liver is the detoxification of the blood since toxic substances or excessive medication can cause damage in the liver structure which can lead to acute liver failure. One example for a medicine which can cause hepatotoxicity is the analgesic Paracetamol (Acetaminophen). The detoxification capability of the liver can be affected by several liver diseases, e.g. the non-alcoholic fatty liver disease (NAFLD). The developed model is an extension of a previos published work, where a multicomponent, poro-elastic multiphasic and multiscale function-perfusion approach based on the Theory of Porous Media (TPM), see [1] has been presented, cf. [2]. Additionally, the decomposition of toxic metabolites causing cell damage is supplemented using the example of Paracetamol. Since the liver has a complex structure and different sizes, a scale bridging approach is requested. The total organ consists of liver lobules, where the toxic metabolites, just like other nutrients and substances, are initiated into the liver with an anisotropic blood flow via the sinusoids. As the structure of the lobules is extremely complex, we use a multicomponent mixture theory based on the Theory of Porous Media (TPM) see [1], to describe the lobule scale. The computational model consists of a tetra-phasic component body, composed of a porous solid structure φ^{S}, fat tissue with the ability of growth φ^{TG}, a liquid phase representing the blood φ^{L} and a solid phase, which characterizes the necrotic cells φ^{N}. The phases $\varphi^{\boldsymbol{\alpha}}$ consist of a carrier phase φ^{α}, also called solvent, and solutes $\varphi^{\alpha\beta}$, representing microscopic components, solved in the solvent and consisting of the nutrients responsible for the liver metabolism. The metabolism takes place in the liver cells, which are located along the sinusoids. To calculate the metabolism processes on the cell scale, an embedded set of coupled ordinary differential equations (ODE) is used.

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